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FORM PTO-1390 (REV. 9-2001) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371	SPM-339-A
	U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 10/019166

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/DE00/02003	June 15, 2000	June 25, 1999

TITLE OF INVENTION
UNIVERSAL TRANSDUCER

APPLICANT(S) FOR DO/EO/US
Meinhard Knoll

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [X] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [X] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [X] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [X] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [ ] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (Unsigned)
10. [X] An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [X] A substitute specification. and Red-line Specification
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [ ] Other items or information:

U.S. APPLICATION NO (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/019166	PCT/DE00/02003	SPM-339-A

21. ☐ The following fees are submitted:	CALCULATIONS PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):	
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1040.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$890.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$740.00**	
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$710.00**	
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890 00
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 130 00

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	28 - 20 =	8	x **$18.00**	$ 144 00
Independent claims	- 3 =		x **$84.00**	$
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$280.00**	$

TOTAL OF ABOVE CALCULATIONS =	$ 1164 00
☒ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. +	$ 582 00
SUBTOTAL =	$ 582 00
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).	$
TOTAL NATIONAL FEE =	$ 582 00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +	$
TOTAL FEES ENCLOSED =	$ 582 00
Amount to be refunded:	$
charged:	$

a. ☒ A check in the amount of $ 582.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 25-0115. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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Darlene P. Condra
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Darlene P. Condra
NAME

37113
REGISTRATION NUMBER

10/019166

531 Rec'd PCT/... 20 DEC 2001

Our Reference: SPM-339-A PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Meinhard Knoll

Serial Number: Concurrent

Filing Date: Concurrent

Examiner/Art Group Unit: Unknown/Unknown

Title: UNIVERSAL TRANSDUCER

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

10019166.022802

Sir:

If any charges or fees must be paid in connection with the following communication, they may be paid out of our Deposit Account No. 25-0115.

Prior to initial examination, please amend the above-identified patent application as indicated below.

In the specification:

Please enter the enclosed Substitute Specification.

In the claims:

1. (Amended) Universal transducer for chemo- and/or biosensor analysis for determining substance concentrations or substance activities in fluids having:

a carrier made of at least a first and a second flat carrier layer;

at least one opening respectively in each of the at least two carrier layers;

at least one continuous cavity which is formed respectively by one opening in each of the at least two carrier layers and extends from a first active surface of the carrier over the first and second carrier layer;

a filling which is disposed in the cavity and is contactable with the analyte in the region of a first active surface of the carrier, and

at least one electrically conductive layer which is disposed at least in part on the surface of one of the at least two carrier layers, which surface is orientated away from the first active surface, in contact with the filling;

the opening in the carrier layer which is orientated away from the first active surface is greater than the opening in the carrier layer which is orientated towards the first active surface.

2. (Amended) Universal transducer according to claim 1, characterized in that the carrier has further flat carrier layers.

3. (Amended) Universal transducer according to claim 2, characterized in that the further flat carrier layers have at least in part further openings which are continuous with at least one of the hollow spaces.

4. (Amended) Universal transducer according to claim 3, characterized in that fillings are disposed in the further openings.

5. (Amended) Universal transducer according to claim 1, characterized in that the at least one filling contains at least one of a substance-detecting membrane and gel.

6. (Amended) Universal transducer according to claim 1, characterized in that there is disposed on the surface of at least the first and the second carrier layers, which are orientated away from the first active surface, at least in part at least one electrically conductive layer respectively.

7. (Amended) Universal transducer according to claim 1, characterized in that at least one of the openings is configured so as to taper conically towards the first active surface.

8. (Amended) Universal transducer according to claim 1, characterized in that the electrically conductive layer extends at least in part towards the lateral walls of the adjacent opening.

9. (Amended) Universal transducer according to claim 1, characterized in that the first active surface in the region of the opening in the carrier layer adjacent to the first active surface is covered with a further membrane, for example with a gas-permeable membrane.

10. (Amended) Universal transducer according to claim 9, characterized in that the further membrane has a thickness of 1 μm up to a few μm.

11. (Amended) Universal transducer according to claim 5, characterized in that the further membrane contains one of polyvinyl chloride (PVC), polyethylene (PE), polyoxymethylene (POM), polycarbonate (PC), ethylene/propylene-Cop (EPDM), polyvinylidene chloride (PVDC), polyvinyl butyral (PVB), cellulose acetate (CA), polypropylene (PP), polymethylmethacrylate (PMMA), polyamide (PA), tetrafluoroethylene/hexafluoropropylene-Cop (FEP), polytetrafluoroethylene (PTFE), phenol formaldehyde (PF), epoxide (EP), polyurethane (PUR), polyester (UP), silicone, melamine formaldehyde (MF), urea formaldehyde (UF), aniline formaldehyde and capton.

12. (Amended) Universal transducer according to claim 9, characterized in that an electrically conductive layer is disposed between the first active surface and the second membrane.

13. (Amended) Universal transducer according to claim 1, characterized in that the cavity on its surface, which is orientated away from the first active surface, is covered with an encapsulation.

14. (Amended) Universal transducer according to claim 13, characterized in that the encapsulation is made of an epoxide resin.

15. (Amended) Universal transducer according to claim 1, characterized in that the openings contain at least in part different fillings.

16. (Amended) Universal transducer according to claim 1, characterized in that a channel carrier with a flow channel and a channel covering thereon are disposed on the first active surface in such a manner that the flow channel is in contact with at least one opening in the carrier layer (1) in the region of the first active surface.

17. (Amended) Universal transducer according to claim 16, characterized in that the thickness of at least one of the channel carrier and the channel covering is a few µm up to a few mm, preferably some µm.

18. (Amended) Universal transducer according to claim 1, characterized in that at least one of the carrier layers contains plastic materials such as polyvinyl chloride (PVC), polyethylene (PE), polyoxymethylene (POM), polycarbonate (PC), ethylene/propylene-Cop (EPDM), polyvinylidene chloride (PVDC), polychlorotrifluorethylene, polyvinyl butyral (PVB), cellulose acetate (CA), polypropylene (PP), polymethylmethacylate (PMMA), polyamide (PA), tetrafluoroethylene/hexafluoropropylene-Cop (FEP), polytetrafluoroethylene (PTFE), phenol formaldehyde (PF), epoxide (EP), polyurethane (PUR), polyester (UP), silicone, melamine formaldehyde (MF), urea formaldehyde (UF), aniline formaldehyde, capton or others or silicon, ceramic or glass.

19. (Amended) Universal transducer according to claim 1, characterized in that the thickness of at least one of the carrier layers is between some few µm up to a few mm, preferably some 100 µm.

20. (Amended) Universal transducer according to claim 1, characterized in that at least one of the electrically conductive layers is made of metals, especially noble metals such as platinum, gold and silver or metal alloys or screen printing pastes, for example based on graphite or metallic materials.

21. (Amended) Universal transducer according to claim 1, characterized in that the thickness of at least one of the electrically conductive layers is 1 µm up to some µm.

22. (Amended) Universal transducer according to claim 5, characterized in that if the filling is a membrane, the filling contains at least one of PVC, silicone, polyurethane and the like one if the filling is a gel, the filling contains at least one of gelatin and polyvinyl alcohol (PVA) or the like.

23. (Amended) Universal transducer according to claim 1, characterized in that the filling contains biocomponents such as at least one of enzymes, micro organisms and antibodies.

24. (Amended) Universal transducer according to claim 1, characterized in that the diameter of at least one of the openings of the carrier layer adjacent to the first active surface on the first active surface is a few µm up to a few mm, preferably some 10 - 100 µm.

25. (Amended) Universal transducer according to claim 1, characterized in that the carrier has two cavities, a filling being disposed in each of the cavities, the filling of the one cavity being in contact with a first electrically conductive layer as reference electrode and the filling of the second cavity being in contact with second or third conductive layers, which are disposed on different carrier layers, as the operating electrode or counter electrode which are subject to a current, and the first, second and third conductive layer forming a three electrode arrangement for amperometric measurements.

26. (Amended) Universal transducer according to claim 25, characterized in that the carrier has a third cavity, in which a filling is disposed which is contact with a further electrically conductive layer which forms a potentiometric electrode and is measurable against the reference electrode.

27. (Amended) Use of universal transducers according to claim 1, as at least one of reference electrode, a sensor element for potentiometric determination and a sensor element for amperometric determination of analyte concentrations or ion activities.

28. (Amended) Use according to claim 27, for one of determining the concentration of at least one of dissolved carbon dioxide, oxygen, glucose and other metabolites and urea and for determining the pH value or other parameters.

REMARKS

After entry of this amendment, claims 1-28 have been amended.

A handwritten, corrected copy of the specification is enclosed showing the changes which have been made to the specification as required by Section 608.01(Q) and 714.20(1) of the Manual of Patent Examining Procedure. The Substitute Specification filed herewith has been amended to utilize idiomatic English, correct minor typographical and grammatical errors and to conform the application to current United States patent practice. The Substitute Specification includes no new subject matter; but does include the same changes handwritten in red in the attached, corrected, original specification. Entry of the Substitute Specification is respectfully requested.

It is submitted that this Amendment has antecedent basis in the application as originally filed, including the specification, claims and drawings, and that this Amendment does not add any new subject matter to the application. Consideration of the application as amended is requested.

Respectfully submitted,

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Dated: December 20, 2001
DPC/jas

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) Universal transducer for chemo- and/or biosensor analysis for determining substance concentrations or substance activities in fluids having:

a carrier made of at least a first [(1)] and a second [(2)] flat carrier layer;

at least one opening [(4.1 - 4.5, 5.1 - 5.5)] respectively in each of the at least two carrier layers [(1,2)];

at least one continuous cavity which is formed respectively by one opening [(4, 5)] in each of the at least two carrier layers and extends from a first active surface of the carrier over the first and second carrier layer [(1, 2)];

a filling [(9)] which is disposed in the cavity and is contactable with the analyte in the region of a first active surface [(10)] of the carrier, and

at least one electrically conductive layer [(8 or 7)] which is disposed at least in part on the surface of one of the at least two carrier layers [(1, 2)], which surface is orientated away from the first active surface [(10)], in contact with the filling [(9)];

the opening in the carrier layer [(2)] which is orientated away from the first active surface [(10)] is greater than the opening in the carrier layer [(1)] which is orientated towards the first active surface [(10)].

2. (Amended) Universal transducer according to [the preceding] claim 1, [characterised] characterized in that the carrier has further flat carrier layers [(3)].

3. (Amended) Universal transducer according to [the preceding] claim 2, [characterised] characterized in that the further flat carrier layers [(3)] have at least in part further openings [(6.1 - 6.5)] which are continuous with at least one of the hollow spaces.

4. (Amended) Universal transducer according to [the preceding] claim 3, [characterised] characterized in that fillings [(9)] are disposed in the further openings [(6.1 - 6.5)].

5. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the at least one filling [(9) or fillings contain] contains at least one of a substance-detecting membrane [and/or] and gel.

6. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that there is disposed on the surface of at least the first [(1),] and the second [(2) and/or the further (3)] carrier layers, which are orientated away from the first active surface [(10)], at least in part at least one electrically conductive layer [(7, 8)] respectively.

7. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that at least one of the openings [(4)] is configured so as to taper conically towards the first active surface [(10)].

8. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the electrically conductive layer [(7, 8)] extends at least in part towards the lateral walls of the adjacent opening [(4, 5)].

9. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the first active surface [(10)] in the region of the opening in the carrier layer [(1)] adjacent to the first active surface [(10)] is covered with a further membrane [(13)], for example with a gas-permeable membrane.

10. (Amended) Universal transducer according to [the preceding] claim 9, [characterised] characterized in that the further membrane [(13)] has a thickness of 1µm up to a few µm.

11. (Amended) Universal transducer according to [one of the two preceding claims] claim 5, [characterised] characterized in that the further membrane [(13)] contains one of polyvinyl chloride (PVC), polyethylene (PE), polyoxymethylene (POM), polycarbonate (PC), ethylene/propylene-Cop (EPDM), polyvinylidene chloride (PVDC), polyvinyl butyral (PVB), cellulose acetate (CA), polypropylene (PP), polymethylmethacrylate (PMMA), polyamide (PA), tetrafluoroethylene/hexafluoropropylene-Cop (FEP), polytetrafluoroethylene (PTFE), phenol formaldehyde (PF), epoxide (EP), polyurethane (PUR), polyester (UP), silicone, melamine formaldehyde (MF), urea formaldehyde (UF), aniline formaldehyde [or] and capton.

12. (Amended) Universal transducer according to [one of the three preceding claims] claim 9, [characterised] characterized in that an electrically conductive layer [(14)] is disposed between the first active surface [(10)] and the second membrane [(13)].

13. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the cavity on its surface, which is orientated away from the first active surface [(10)], is covered with an encapsulation [(11)].

14. (Amended) Universal transducer according to [the preceding] claim 13, [characterised] characterized in that the encapsulation [(11)] is made of an epoxide resin.

15. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the openings contain at least in part different fillings [(9, 9.3, 9.31)].

16. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that a channel carrier [(18)] with a flow channel [(20)] and a channel covering [(19)] thereon are disposed on the first active surface [(10)] in such a manner that the flow channel [(20)] is in contact with at least one opening [(4.1 - 4.3)] in the carrier layer (1) in the region of the first active surface [(10)].

17. (Amended) Universal transducer according to [the preceding] claim 16, [characterised] characterized in that the thickness of at least one of the channel carrier [(18) and/or of] and the channel covering [(19)] is a few µm up to a few mm, preferably some µm.

18. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that at least one of the carrier layers [(1, 2, 3)] contains plastic materials such as polyvinyl chloride (PVC), polyethylene (PE), polyoxymethylene (POM), polycarbonate (PC), ethylene/propylene-Cop (EPDM), polyvinylidene chloride (PVDC), polychlorotrifluorethylene, polyvinyl butyral (PVB), cellulose acetate (CA), polypropylene (PP), polymethylmethacylate (PMMA), polyamide (PA), tetrafluoroethylene/hexafluoropropylene-Cop (FEP), polytetrafluoroethylene (PTFE), phenol formaldehyde (PF), epoxide (EP), polyurethane (PUR), polyester (UP), silicone, melamine formaldehyde (MF), urea formaldehyde (UF), aniline formaldehyde, capton or others or silicon, ceramic or glass.

19. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the thickness of at

least one of the carrier layers [(1, 2, 3)] is between some few µm up to a few mm, preferably some 100 µm.

20. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that at least one of the electrically conductive layers [(7, 8)] is made of metals, especially noble metals such as platinum, gold and silver or metal alloys or screen printing pastes, for example based on graphite or metallic materials.

21. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the thickness of at least one of the electrically conductive layers [(7, 8)] is 1 µm up to some µm.

22. (Amended) Universal transducer according to [one of the preceding claims] claim 5, [characterised] characterized in that if the filling [(9) as] is a membrane , the filling contains at least one of PVC, silicone, polyurethane and the like [and/or as] one if the filling is a gel [(9)], the filling contains at least one of gelatin [or] and polyvinyl alcohol (PVA) or the like.

23. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the filling contains biocomponents such as at least one of enzymes, micro organisms [and/or] and antibodies.

24. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the diameter of at least one of the openings [(4.1 - 4.5)] of the carrier layer [(1)] adjacent to the first active surface [(10)] on the first active surface [(10)] is a few µm up to a few mm, preferably some 10 - 100 µm.

25. (Amended) Universal transducer according to [one of the preceding claims] claim 1, [characterised] characterized in that the carrier has two cavities [(4.2, 5.2, 6.2, and 4.4, 5.4, 6.4)], a filling being disposed in each of the cavities, the filling of the one cavity being in contact with a first electrically conductive layer as reference electrode and the filling of the second cavity being in contact with second or third conductive layers, which are disposed on different carrier layers, as the operating electrode or counter electrode which are subject to a current, and the first, second and third conductive layer forming a three electrode arrangement for amperometric measurements.

26. (Amended) Universal transducer according to [the preceding claim] claim 25, [characterised] characterized in that the carrier has a third cavity, in which a filling is disposed which is contact with a further electrically conductive layer which forms a potentiometric electrode and is measurable against the reference electrode.

27. (Amended) Use of universal transducers according to [at least one of the preceding claims] claim 1, as at least one of reference electrode, [as] a sensor element for potentiometric determination [and/or as] and a sensor element for amperometric determination of analyte concentrations or ion activities.

28. (Amended) Use according to [the preceding] claim 27, for one of determining the concentration of at least one of dissolved carbon dioxide, oxygen, glucose [and/or] and other metabolites [and/or] and urea [or] and for determining the pH value or other parameters.

Substitute Spec

Our Referenc PATENT

TRANSDUCER

BACKGROUND OF THE INVENTION

[0001] The present invention relates to a universal transducer and also chemo- and biosensors based on miniaturized universal transducers of this type. Sensors of this type are used for example in chemical analysis or in medical diagnosis for determining substance concentrations or ion, activities in fluids.

[0002] According to the state of the art, chemo- and biosensor elements are produced based on carriers with metal contacts and membrane or gel materials which are specific for the respective analyte. On ion-selective electrodes, potential differences are thereby measured according to the potentiometric measuring principle against a reference electrode. In amperometric sensors, currents between operating and reference electrodes or counter electrodes are determined after application of an electrical voltage according to the two electrode or three electrode principle (see Friedrich Oehme, Chemical Sensors, Vieweg Press 1991).

[0003] P 41 15 414 discloses chemo- and biosensors of this type which are extremely miniaturized. Cavities are thereby integrated in carriers made of semiconductor materials such as silicon, said cavities being covered with a metal film on their internal surface and containing the respective substance-detecting membrane- or gel materials.

[0004] It is however disadvantageous in the state of the art that the carriers for such sensors can only be provided with two different metal films, for example for amperometric measurements, if these metal films are structured photolithographically in depth on the three-dimensional surface of the cavities. Even when the electrically conductive film is not allowed to come into direct contact with the measuring medium, the internal surface of the cavity in the contact region must be structured photolithographically with the measuring medium in order not to apply any metal film in this contact region. Three-dimensionally photolithographic

structuring methods of this type imply however a significant technological complexity and cost.

[0005] A further disadvantage of this state of the art is that, with the sensor elements disclosed there, it has not been possible to date to operate amperometric and potentiometric sensor elements together on only one single carrier. For, in the case of the state of the art, both the amperometric and also the potentiometric sensor elements are in contact with the same measuring medium and the electrical currents of the amperometric sensors flow over the interface between the membrane and the measuring medium. The potential measurements of the adjacent potentiometric sensors are thereby disturbed.

SUMMARY OF THE INVENTION

[0006] It is therefore the object of the present invention to make available a universal transducer which is simple to produce and which permits a three-dimensional structuring of the transducer by simple means. These universal transducers should furthermore be suitable in order to use amperometric and potentiometric sensors for determining the same fluid at the same time.

[0007] According to the invention, the universal transducer has a carrier which comprises at least two flat carrier layers. A cavity extends by means of openings through these carrier layers and can be contacted on one side of the carrier with the analyte. The sides of the carrier layers which are orientated away from this contact surface are provided with electrically conductive layers or films as electrodes. The cavity itself is filled with a filling which can contain a substance-detecting membrane and/or gel, for example an ion-selective membrane. According to the invention, it is therefore possible with such a structure to build up the individual carrier layers and electrodes successively, as a result of which a three-dimensional photolithographical structuring can be dispensed with. Therefore a transducer can be produced for example without special photolithographic structuring, the electrodes of said transducer not coming into contact with the measuring medium. If the transducer has only one electrically conductive layer, then this can be disposed on one of the carrier

layers which is further away from the first active surface, while the carrier layer which forms the first active surface has no electrically conductive layer. As a result, a contact between the electrically conductive layer and the measuring medium can be avoided in a simple manner. In total, it is possible to dispose the electrodes, in contrast to the state of the art, three-dimensionally in the direction of the depth of the universal transducer. Furthermore, it is also possible to provide a plurality of such cavities as universal transducers on the same carrier in order to produce for example a plurality of amperometric or a plurality of potentiometric sensors or even amperometric and potentiometric sensors for the same measuring medium at the same time on the same carrier.

[0008] The difference between potentiometric and amperometric sensor elements lies thereby simply in the locally selective application of the electrode layers, for example by sputtering with the help of shadow masks.

[0009] In particular, the structure of the amperometric and potentiometric sensors for the most varied of analytes is effected according to a uniform principle, very different sensor elements being able to be produced however simultaneously. The carrier layers for different sensor elements differ thereby possibly only by the configuration of the openings in the individual carrier layers. As the electrode layers and also the fillings can be applied in a locally selective manner, for example via the insertion of different substance-detecting materials in the cavities in the region of the respective openings, a vertical structure of the individual sensor systems is possible.

[0010] In this way, universal transducers can therefore also be produced, the further formation of which into multi-sensors with different sensor element types can also be decided later.

[0011] The carrier layers of the universal transducer according to the invention are advantageously made of plastic materials such as polyvinyl fluoride, polyethylene, polyoxymethylene, polycarbonate, ethylene/propylene-COP, polyvinylidene chloride, polychlorotrifluoroethylene, polyvinyl butyral, cellulose acetate, polypropylene, polymethylmethacrylate, polyamide, tetrafluoroethylene/hexafluoropropylene-COP, polytetrafluoroethylene, phenol

formaldehyde, epoxide, polyurethane, polyester, silicone, melamine formaldehyde, urea formaldehyde, aniline formaldehyde, capton or the like or also made of silicon, ceramic or glass. The universal transducer according to the invention can hence be produced based on different production technologies, such as plastic material injection moulding technology, plastic material film technology, ceramics te chnology or even silicon technology.

[0012] The electrically conductive layers can comprise metals, in particular noble metals such as platinum, gold or silver or even metal alloys or screen printing pastes, for example based on graphite or metallic materials.

[0013] The fillings are produced advantageously from materials which are known conventionally for ion-selective membranes, such as for example, PVC, silicone, polyurethane or the like. For the gel fillings there are used for example gelatine or polyvinyl alcohol or the like.

[0014] The encapsulation can advantageously comprise materials which are compatible with the materials of the membranes or gels, for example epoxide resins.

[0015] For the further membrane, which covers the measuring window of a diameter in the region of a first active surface, for example a gas-permeable membrane, very thin materials are used preferably, in the range of 1 μm up to a few micrometers, advantageously the materials polyvinyl fluoride, polyethylene, polyoxymethylene, polycarbonate,ethylene/propylene-COP, polyvinylidene chloride, polychlorotrifluoroethylene, polyvinyl butyral, cellulose acetate, polypropylene, polymethylmethacrylate, polyamide, tetrafluoroethylene/hexafluoropropylene-COP, polytetrafluoroethylene, phenol formaldehyde, epoxide, polyurethane, polyester, silicone, melamine formaldehyde, urea formaldehyde, silicone, aniline formaldehyde, capton or the like. These further membranes are glued advantageously on the first active surface of the first carrier layer or are poured from the liquid phase.

[0016] The thicknesses of the individual carrier layers can be between a few μm up to a few mm, preferably in the range of less than 100 μm. The apertures of the openings (measuring windows) in the first carrier layer in the region of the first active surface are likewise advantageously in the range of a few μm to a few mm,

preferably some 10 to 100 μm. The thicknesses of the electrically conductive layers which are applied as electrodes on the surfaces of the individual carrier layers, which surfaces are orientated away from the first active surface, are in the range of a few μm.

[0017] The flow channels provided in an advantageous embodiment forming channel carriers and channel coverings, which bring the liquid with the analyte to the individual measuring windows, comprise advantageously the same materials as the individual carrier layers. The channel carrier and the channel covering have thereby thicknesses of a few gm to a few mm, preferably some 100 μm.

[0018] According to the respective choice of material, the shaping of the carrier layers is effected by different methods. If the carrier layers axe made for example of silicon, then the production of the openings can be effected by the method of deep etching. Etching media such as KOH or dry etching methods are used hereby for example. Openings are thereby produced which can have different cross-sections, for example square, rectangular or round. In the case of anisotropic etching, openings are produced thereby in the shape of a truncated pyramid which taper from one side of the carrier layer to the other side of the carrier layer, for example in the direction of the first active surface.

[0019] When using plastic materials for the carrier layers, these can be produced by injection moulding. The openings are hereby caused by the shaping of the injection moulding tool. However it is also possible to use flat carrier materials, for example plastic material films for the individual carrier layers, which are then provided with openings by cutting, boring, micro-imprinting or etching methods. Advantageously, laser cutting can also be used.

[0020] The electrically conductive layers axe applied on the carrier layers with known methods of thin layer technology by evaporation coating in the vacuum or by sputtering. The structuring can thereby occur in that evaporation coating or sputtering is produced by shadow masks. In addition, the use of photolithography is nevertheless possible, however for producing the transducers according to the invention there being no need for structuring in depth in a three-dimensional manner

at all. It is likewise possible to produce the electrically conductive electrodes by means of the screen printing method or by electrolytic deposition.

[0021] The fillings of the openings, for example made of membranes or gels, are advantageously introduced into the cavities by means of an automatic dispensing device. This method is also suitable for applying the encapsulation, which however can also be applied with the screen printing method.

[0022] In order to produce the transducers according to the invention, first of all the carrier layers are provided with openings and then electrically conductive layers, are applied if necessary individually respectively. The electrically conductive layers can also be applied before the production of the openings.

[0023] Then the carrier layers and possibly the channel carrier and the channel covering are placed one above the other and joined to each other. For the purpose of joining, various materials and methods are used according respectively to the material of the carrier layers and of the channel carrier or the channel covering. If the carrier layers and the channel carrier/channel covering are made of silicon materials, then conventional bonding methods can be used, for example anodic bonding for joining the individual layers. In addition, joining of the carrier layers is also possible by means of gluing techniques. When using plastic materials for the carrier layers, the channel carrier and the channel covering, these can likewise be glued. When using film materials it is again possible to join the various layers to each other as films by lamination, for example by hot lamination or by means of otherwise known sealing methods.

[0024] According to the invention, a universal transducer is thus proposed which has a simple construction and enables various measuring methods (amperometry, potentiometry) on the same carrier and with the same measuring solution. This carrier is distinguished by the fact that it is structured in depth. Because of the layer-like structure, in which first of all individual carrier layers are produced, are provided with openings, possibly coated with electrically conductive layers or first coated and then provided with openings and then the individual carrier layers are disposed one above the other and are joined to each other in such a manner

that the individual openings produce vertical continuous cavities and then these cavities are filled with suitable fillings, for example substance-detecting membranes or gels, a simple production of three-dimensionally structured universal transducers of this type according to the invention is possible.

[0025] Adhesion agents, for example chrome, can be applied between the carrier I layers and the electrically conductive layers. Between the electrically conductive layers and the fillings of the openings there can be introduced further layers, for example anti-interference layers, for example made of cellulose acetate, polyurethane or the like.

BRIEF DESCRIPTION OF THE DRAWINGS

[0026] A few examples of the present universal transducers according to the invention are described subsequently.

There are shown

[0027] Fig. 1 a universal transducer with a plurality of sensor elements;

[0028] Fig. 2 various glucose sensors;

[0029] Fig. 3 various ion-selective electrodes;

[0030] Fig. 4 various sensor elements;

[0031] Fig. 5 a CO_2 sensor according to the invention;

[0032] Fig. 6 an amperometric glucose sensor with flow channel; and

[0033] Fig. 7 a universal transducer with a plurality of sensor elements and a flow channel.

DESCRIPTION OF THE PREFERRED EMBODIMENT

[0034] In the following embodiments and Figures, the same elements are designated respectively with the same reference numbers. If in one described universal transducer a plurality of sensors (for example I, II, III, IV, V in Fig. 1) are described with the same elements with respect to type or function (for example filling 9) then the reference numbers for these elements which are the same in type or function are

assigned to the sensor elements designated respectively with Roman numerals (I - V) by a number after a point (for example 9.1, 9.2 ,...., 9.5).

[0035] Figure 1 shows a carrier which comprises a first carrier layer 1, a second carrier layer 2 and a third carrier layer 3 which are all joined together securely. These carrier layers 1 to 3 are configured by means of openings 4 to 6 and also by means of electrically conductive layers 7 and 8 such that various sensor elements I to V are produced in the regions of the openings. In the carrier layer I there are situated openings 4 (4.1 for the sensor element I, 4.2 for the sensor element II etc.), in the carrier layer 2 there are situated openings 5 (5.1 - 5.5) and in the carrier layer 3 openings 6 (6.1 - 6.5). The openings of the carrier layers 1 to 3 are situated in such a manner one above the other that cavities are produced which extend over the three carrier layers.

[0036] An electrically conductive film 7 was applied in part on the surface of the carrier layer 1 and another electrically conductive film 8 on the carrier layer 2. The openings 4 to 6 serve as cavities for receiving fillings 9 (membrane or gel materials). After introduction of the fillings 9, the cavities are sealed by means of an encapsulating material 11. In the opening of the first carrier layer, there is produced one active sensor surface 10 respectively on the external phase boundary of the filling 9.

[0037] A platinum film 7 was produced on the first carrier layer and a silver film on the carrier layer 2 as electrically conductive layers.

[0038] On the basis of such a universal transducer, very different sensor elements can be produced.

[0039] The element I represents a reference electrode for the other sensor elements. The silver film 8.1 can be chloridated at its interface to the filling 9.1. For example KCl solution in gelatine or in polyvinyl alcohol (PVA) is introduced here from above as a filling 9.1. Such an element corresponds to a conventional Ag/AgCl reference electrode. Such a reference electrode can be used for example together with an ion selective electrode (ISE).

[0040] Such an ion-selective electrode (ISE) is produced as sensor element II. This sensor element II is constructed in the same manner as the element 1. However, the cavity here in the region of the openings 4.2, 5.2 and 6.2 is filled with an ion-selective membrane is selective membrane 9.2. This ion-selective membrane is made for example of PVC material or silicone which in addition to a softener and additives also contains an ionophore as an electroactive substance. The PVC membrane 9.2 is in direct contact with the metal film 8.2 (Ag). If a liquid measuring medium interacts with the ion-selective membrane 9.2 in the region of the measuring window 10.2, then a potential difference is formed in the region of the measuring window which can be measured against the reference electrode I which is itself in contact with the measuring medium in the region of the measuring window 10.1.

[0041] The element III shows another potentiometric sensor element which can be used for determining urea. First of all an ion-selective membrane 9.3 for determining ammonium is introduced into the cavity in the region of the openings 5.3 and 6.3 from the direction of the opening 4.3 of the carrier layer 1 or from the opening 6.3 of the carrier layer 3. Such an ion-selective membrane can once again be produced from PVC material with a softener and additives and also with an ionophore for ammonium. Next, a second membrane 9.3.1 is applied to the membrane 9.3 and is made for example of a PCS gel (polycarbamoyl sulfonate) which contains the enzyme urease as biocomponent. During measurement, the liquid measuring medium interacts with the analyte urea in the region of the measuring window 10.3 with the membrane 9.3.1. The urea molecules are converted catalytically by the urease enzyme. The thereby changing ammonium concentration in the membrane 9.3.1 can be detected by means of the ion-selective ammonium membrane 9.1 Measurement is effected against the reference electrode 1. For this purpose, the potential of the urea sensor is measured at the silver film 8.3. The metal film 8.3 extends perpendicularly to the plane of the picture and lies externally freely (12.5) analogously to the metal film 8.5 of the sensor element V. The electrical connection can occur here.

[0042] A glucose sensor is produced as sensor element IV. The cavity in the region of the openings 4.4, 5.4 and 6.4 is filled here with PVA which contains the enzyme glucose oxidase (GOD). If glucose from the measuring medium in the region of the measuring window 10.4 interacts with the membrane material 9.4, then the glucose is converted catalytically by means of the enzyme GOD. H_2O_2 is thereby produced. This H_2O_2 can be electrochemically converted amperometrically on the Pt electrode 7.4. This takes place according to the amperometric measuring principle in which the electrical current is measured between the Pt electrode 7.4 and the Ag/AgCl electrode 8.4. The measurement can be effected in the described manner by means of a two electrode arrangement.

[0043] If measurement with potentiometric sensor elements (for example sensor elements II and III) is intended to be effected simultaneously, then it is particularly advantageous because of the configuration of the universal transducer to implement a three electrode measurement in which the potential of the Pt operating electrode 7.4 is determined by means of the reference electrode I. The current of the sensor element IV thereby flows over the Ag/AgCl counter electrode 8.4.

[0044] As operating and counter elecrode are disposed according to the invention vertically in a cavity and the reference electrode I comes into contact with the measuring medium above the measuring window 10.1 outwith the cavity of the sensor element IV, the electrical current cannot flow over the measuring window 10.4 and over the measuring medium and hence cannot disturb the measurements at the potentiometric sensor elements.

[0045] In an analogous manner to the glucose sensor IV, a sensor element V is produced for determining concentrations of dissolved oxygen in the liquid measuring medium. The cavity in the region of the openings 4.5, 5.5 and 6.5 is filled here with a KCI solution or a KCI gel. The opening 4.5 in the carrier layer 1 is covered with a gas-permeable membrane 13. The oxygen dissolved in the liquid measuring medium can diffuse through the gas-permeable membrane and is converted electrochemically at the platinum electrode 7.5 according to the amperometric measuring principle. For this purpose, the electrical current between the platinum electrode 7.5 and the

Ag/AgCl electrode 8.5 is measured after the application of an electrical voltage of some 100 mV.

[0046] Figure 2 a) shows the sensor element IV from Figure 1. Another geometry of the opening 4 in the carrier layer 1 is illustrated in Figure 2 b). Here, the electrically conductive film 7 extends into the region of the opening. This can be achieved in that the film 7 is applied after producing the opening for example by evaporation coating in the vacuum or by sputtering. A similar arrangement is shown in Figure 2 c). Here, the film 7 however does not extend into the region of the internal surface of the opening 4. All three sensor elements are suitable for amperometric measurements. The fillings 9 can contain membrane or gel materials, according respectively to the configuration of the sensor element, and also the most varied biocomponents, as are commonly used here in biosensor analysis. These can be enzymes, microorganisms or antibodies.

[0047] This arrangement of the metal films 7 on the carrier layers 1 makes it possible to produce transducer structures in which the films 7 extend up to the measuring windows 10 or not, according to the configuration of the sensor elements.

[0048] In Figure 3, various embodiments of the transducer are illustrated, as are illustrated for ion-selective electrodes according to the example II of Figure 1 or reference electrodes according to the example I of Figure 1. Analogously to the openings in the carrier layer 1 of Figure 2, the openings in this example in the carrier layer 2 are configured differently. Here, the electrically conductive layers 8 extend respectively up to the carrier layer 1 (Fig. 3 a) and b)). In Figure 3 c), the electrically conductive layer 8 is located only on the flat surface of the carrier layer 2.

[0049] This arrangement of the metal films 8 on the carrier layers 2 makes it possible to produce transducer structures in which the films 8 have a greater or smaller spacing from the carrier layer 1 and from the measuring window 10 according to the configuration of the sensor element.

[0050] If reference electrodes are produced in accordance with the element I of Figure 1, then the electrically conductive layers 8 in Figures 3 a) to c) are made for example of a chloridated silver film. The filling 9 of the cavity in the carrier layers 1

to 3 is made here also of a KC1 gel. It is likewise possible to configure ion-selective electrodes with polymer membranes based on the structures according to Figure 3. For this purpose, the electrically conductive layers 8 are produced for example from silver. The fillings 9 of the cavities in the region of the openings 4, 5 and 6 are made in the examples according to Figure 3 a) and b) for example of PVC, silicone or other materials for ion-selective membranes and are provided with the necessary active components.

[0051] An ion-selective electrode with an internal electrolyte is illustrated in Figure 3 c). First of all an ion-selective membrane 9.1 is filled from the top into the cavity in the region of the openings 4 and 5. This membrane has itself no contact with an electrically conductive layer. A KC1 gel 9 is applied over the ion-selective membrane. This KC1 gel 9 is in direct contact with the chloridated silver layer 8.

[0052] In the examples according to Figure 4, additional membranes 13 are introduced respectively into the sensor elements. Figure 4 a) shows for example a glucose sensor element which is sealed with a polyurethane (PU) membrane to the measuring window 10. This polyurethane membrane is firmly joined to the carrier layer 1. The electrode layer 14 made of platinum is firmly joined to the membrane 13 and the carrier layer 2. The filling 9 is made here for example of PVA with the enzyme GOD. The filling 9 is in direct contact with a reference electrode layer or a counter electrode layer 8 which is made of a chloridated silver film.

[0053] In a similar manner to this glucose sensor according to Figure 4 a), an oxygen sensor element can be produced. Instead of the PU membrane 13 there occurs here a gas-permeable membrane made of for example Teflon or silicone. The filling 9 is made in this case of a KC1 solution or a KC1 gel.

[0054] A further variant of a glucose sensor is illustrated in Figure 4 b). In contrast to Figure 4 a), here the platinum operating electrode 15 is located directly on the carrier layer 1. The membrane 13 is made here likewise of polyurethane.

[0055] A further variant of an oxygen sensor is illustrated in Figure 4 c). In contrast to Figure 4 a), the platinum electrode layer 14 is located only under the carrier layer 2.

[0056] Based on Figures 4 a) and 4 c), sensors for measuring concentrations of the dissolved carbon dioxide can also be produced in liquid measuring media. Such sensors operate according to the Severinghaus principle. The membrane 13 is made here of gas-permeable material. The filling 9 is an electrolyte gel. The electrode layers 14 are made of iridium oxide which is a pH-sensitive material.

[0057] During measurement, the carbon dioxide diffuses through the gas-permeable membrane 13. This changes the pH value in the electrolyte filling 9 which can be measured by means of the pH-sensitive iridium oxide electrode 14 against the reference electrode comprising the chloridated silver, film 8.

[0058] A CO_2 sensor is illustrated in Figure 5 as a further embodiment. A silver layer 8 and a chloridated silver layer 14 are applied here to the carrier layer 2. After production of the transducer, the cavity in the region of the openings 5 and 6 is filled with a pH-sensitive polymer membrane (for example made of PVC) so that, in conjunction with the silver layer 8, an ion-selective electrode is formed for the pH value. Next, the encapsulation layer 11 is applied. An internal electrolyte 16 is applied to the pH-sensitive membrane and is in contact both with the surface of the pH-sensitive membrane 9 and also with the surface of the chloridated silver layer 14. A gaspermeable membrane 13, which is made for example of silicone, is poured on the internal electrolyte layer 16. The internal electrolyte also fills the reservoir 16A. This extends the service-life of the sensor.

[0059] In this manner, a sensor for measuring CO_2 concentrations in aqueous media is produced according to the Severinghaus principle. During measurement, the carbon dioxide diffuses through the gas-permeable membrane 13. This changes the pH value in the electrolyte layer 16 which can be measured by means of the ion-selective electrode, comprising the ion-selective membrane 9 and the silver layer 8, against the reference electrode which is made of the chloridated silver film 14.

[0060] A sensor element according to example IV of Figure 1 is illustrated once again in Figure 6 as a further embodiment. In addition, a flow channel 20 is integrated here. For this purpose, a channel carrier 18 is applied to the carrier layer 1 and contains recesses for the flow channel 20. The channel carrier 18 is closed by

means of a channel covering 19. In this manner, flow channels 20 can be produced with very small cross-sections. It is likewise possible to connect various sensor elements (such as are illustrated for example in Figure 1) with the same channel.

[0061] In analogy to and extension of Figure 6, an embodiment is illustrated in Figure 7 with a through-flow channel 20. This example was derived from Figure 1. Instead of the sensor elements I and V, there are located here now the connections 21 and 22 for the supply and discharge of the liquid measuring medium. The liquid measuring medium enters into the channel 20 which comprises the channel carrier 18 and the covering 19. In this example, the element II can be a reference electrode with a chloridated silver electrode 8.2 which contains a filling 9.2 made of a KC1 gel. The sensor element at the position III is, as in the example according to Figure 1, a urea sensor, while at position IV a glucose sensor is situated. The urea sensor III is measured against the reference electrode II according to the potentiometric measuring method. The glucose sensor IV is measured according to the three electrode principle. For this purpose, the platinum electrode 7.4 is used as operating electrode. The silver film 8.4 serves as a counter electrode which can be subject to a current while the reference electrode II serves for adjusting the polarisation voltage of the operating electrode 7.4.

ABSTRACT OF THE DISCLOSURE

[0062] The present application relates to a universal transducer and chemo- and biosensors based on miniaturized universal transducers of this type which are used for example in chemical analysis, medicinal diagnosis and the like for determining substance concentrations or ion activities in fluids.

[0063] The universal transducer according to the invention has a carrier which comprises at least two flat carrier layers, each of the two carrier layers having at least one opening. These openings form a continuous cavity which extends from a first active surface of the carrier over the first and the second carrier layer. On the surfaces of at least one of the two carrier layers, which surfaces are orientated away from the first active surface, there is disposed at least in part one electrically conductive layer which is in contact with a filling of the cavity.

(Figure 2c)

Universal transducer

BACKGROUND OF THE INVENTION (Underline + center)

The present invention relates to a universal transducer and also chemo- and biosensors based on [miniaturised] manufactured universal transducers of this type. Sensors of this type are used for example in chemical analysis or in medical diagnosis for determining substance concentrations or ion activities in fluids.

According to the state of the art, chemo- and biosensor elements are produced based on carriers with metal contacts and membrane or gel materials which are specific for the respective analyte. On ion-selective electrodes, potential differences are thereby measured according to the potentiometric measuring principle against a reference electrode. In amperometric sensors, currents between

operating and reference electrodes or counter electrodes are determined after application of an electrical voltage according to the two electrode or three electrode principle (see Friedrich Oehme, Chemical Sensors, Vieweg Press 1991).

P 41 15 414 discloses chemo- and biosensors of this type which are extremely miniaturised. Cavities are thereby integrated in carriers made of semiconductor materials such as silicon, said cavities being covered with a metal film on their internal surface and containing the respective substance-detecting membrane- or gel materials.

It is however disadvantageous in the state of the art that the carriers for such sensors can only be provided with two different metal films, for example for amperometric measurements, if these metal films are structured photolithographically in depth on the three-dimensional surface of the cavities. Even when the electrically conductive film is not allowed to come into direct contact with the measuring medium, the internal surface of the cavity in the contact region must be structured photolithographically with the measuring medium in order not to apply any metal film in this contact region. Three-dimensionally photolithographic structuring methods of this type imply however a significant technological complexity and cost.

A further disadvantage of this state of the art is that, with the sensor elements disclosed there, it has not been possible to date to operate amperometric and potentiometric sensor elements together on only one single carrier. For, in the case of the state of the art, both the amperometric and also the potentiometric sensor elements are in contact with the same

measuring medium and the electrical currents of the amperometric sensors flow over the interface between the membrane and the measuring medium. The potential measurements of the adjacent potentiometric sensors are thereby disturbed.

SUMMARY OF THE INVENTION

(Underline + Center)

It is therefore the object of the present invention to make available a universal transducer which is simple to produce and which permits a three-dimensional structuring of the transducer by simple means. These universal transducers should furthermore be suitable in order to use amperometric and potentiometric sensors for determining the same fluid at the same time.

[This object is achieved by the universal transducer according to claim 1 and also its usages according to claim 27. Advantageous developments of the universal transducer according to the invention and of uses according to the invention are given in the dependent claims.]

According to the invention, the universal transducer has a carrier which comprises at least two flat carrier layers. A cavity extends by means of openings through these carrier layers and can be contacted on one side of the carrier with the analyte. The sides of the carrier layers which are orientated away from this contact surface are provided with electrically conductive layers or films as electrodes. The cavity itself is filled with a filling which can contain a substance-detecting membrane and/or gel, for example an ion-selective membrane. According to the invention, it is therefore possible with such a structure to build up the individual carrier layers and electrodes successively, as a

result of which a three-dimensional photolithographical structuring can be dispensed with. Therefore a transducer can be produced for example without special photolithographic structuring, the electrodes of said transducer not coming into contact with the measuring medium. If the transducer has only one electrically conductive layer, then this can be disposed on one of the carrier layers which is further away from the first active surface, while the carrier layer which forms the first active surface has no electrically conductive layer. As a result, a contact between the electrically conductive layer and the measuring medium can be avoided in a simple manner. In total, it is possible to dispose the electrodes, in contrast to the state of the art, three-dimensionally in the direction of the depth of the universal transducer. Furthermore, it is also possible to provide a plurality of such cavities as universal transducers on the same carrier in order to produce for example a plurality of amperometric or a plurality of potentiometric sensors or even amperometric and potentiometric sensors for the same measuring medium at the same time on the same carrier.

The difference between potentiometric and amperometric sensor elements lies thereby simply in the locally selective application of the electrode layers, for example by sputtering with the help of shadow masks.

In particular, the structure of the amperometric and potentiometric sensors for the most varied of analytes is effected according to a uniform principle, very different sensor elements being able to be produced however simultaneously. The carrier layers for different sensor elements differ thereby

possibly only by the configuration of the openings in the individual carrier layers. As the electrode layers and also the fillings can be applied in a locally selective manner, for example via the insertion of different substance-detecting materials in the cavities in the region of the respective openings, a vertical structure of the individual sensor systems is possible.

In this way, universal transducers can therefore also be produced, the further formation of which into multi-sensors with different sensor element types can also be decided later.

The carrier layers of the universal transducer according to the invention are advantageously made of plastic materials such as polyvinyl fluoride, polyethylene, polyoxymethylene, polycarbonate, ethylene/propylene-COP, polyvinylidene chloride, polychlorotrifluoroethylene, polyvinyl butyral, cellulose acetate, polypropylene, polymethylmethacrylate, polyamide, tetrafluoroethylene/hexafluoropropylene-COP, polytetrafluoroethylene, phenol formaldehyde, epoxide, polyurethane, polyester, silicone, melamine formaldehyde, urea formaldehyde, aniline formaldehyde, capton or the like or also made of silicon, ceramic or glass. The universal transducer according to the invention can hence be produced based on different production technologies, such as plastic material injection moulding technology, plastic material film technology, ceramics technology or even silicon technology.

The electrically conductive layers can comprise metals, in particular noble metals such as platinum, gold or silver or even metal alloys or screen printing pastes, for example based on graphite or metallic materials.

The fillings are produced advantageously from materials which are known conventionally for ion-selective membranes, such as for example, PVC, silicone, polyurethane or the like. For the gel fillings there are used for example gelatine or polyvinyl alcohol or the like.

The encapsulation can advantageously comprise materials which are compatible with the materials of the membranes or gels, for example epoxide resins.

For the further membrane, which covers the measuring window of a diameter in the region of a first active surface, for example a gas-permeable membrane, very thin materials are used preferably, in the range of 1 μm up to a few micrometers, advantageously the materials polyvinyl fluoride, polyethylene, polyoxymethylene, polycarbonate, ethylene/propylene-COP, polyvinylidene chloride, polychlorotrifluoroethylene, polyvinyl butyral, cellulose acetate, polypropylene, polymethylmethacrylate, polyamide, tetrafluoroethylene/hexafluoropropylene-COP, polytetrafluoroethylene, phenol formaldehyde, epoxide, polyurethane, polyester, silicone, melamine formaldehyde, urea formaldehyde, silicone, aniline formaldehyde, capton or the like. These further membranes are glued advantageously on the first active surface of the first carrier layer or are poured from the liquid phase.

The thicknesses of the individual carrier layers can be between a few μm up to a few mm, preferably in the range of less than 100 μm. The apertures of the openings (measuring

windows) in the first carrier layer in the region of the first active surface are likewise advantageously in the range of a few µm to a few mm, preferably some 10 to 100 µm. The thicknesses of the electrically conductive layers which are applied as electrodes on the surfaces of the individual carrier layers, which surfaces are orientated away from the first active surface, are in the range of a few µm.

The flow channels provided in an advantageous embodiment forming channel carriers and channel coverings, which bring the liquid with the analyte to the individual measuring windows, comprise advantageously the same materials as the individual carrier layers. The channel carrier and the channel covering have thereby thicknesses of a few µm to a few mm, preferably some 100 µm.

According to the respective choice of material, the shaping of the carrier layers is effected by different methods. If the carrier layers are made for example of silicon, then the production of the openings can be effected by the method of deep etching. Etching media such as KOH or dry etching methods are used hereby for example. Openings are thereby produced which can have different cross-sections, for example square, rectangular or round. In the case of anisotropic etching, openings are produced thereby in the shape of a truncated pyramid which taper from one side of the carrier layer to the other side of the carrier layer, for example in the direction of the first active surface.

When using plastic materials for the carrier layers, these can be produced by injection moulding. The openings are hereby

caused by the shaping of the injection moulding tool. However it is also possible to use flat carrier materials, for example plastic material films for the individual carrier layers, which are then provided with openings by cutting, boring, micro-imprinting or etching methods. Advantageously, laser cutting can also be used.

The electrically conductive layers are applied on the carrier layers with known methods of thin layer technology by evaporation coating in the vacuum or by sputtering. The structuring can thereby occur in that evaporation coating or sputtering is produced by shadow masks. In addition, the use of photolithography is nevertheless possible, however for producing the transducers according to the invention there being no need for structuring in depth in a three-dimensional manner at all. It is likewise possible to produce the electrically conductive electrodes by means of the screen printing method or by electrolytic deposition.

The fillings of the openings, for example made of membranes or gels, are advantageously introduced into the cavities by means of an automatic dispensing device. This method is also suitable for applying the encapsulation, which however can also be applied with the screen printing method.

In order to produce the transducers according to the invention, first of all the carrier layers are provided with openings and then electrically conductive layers are applied if necessary individually respectively. The electrically conductive layers can also be applied before the production of the openings.

Then the carrier layers and possibly the channel carrier and the channel covering are placed one above the other and joined to each other. For the purpose of joining, various materials and methods are used according respectively to the material of the carrier layers and of the channel carrier or the channel covering. If the carrier layers and the channel carrier/channel covering are made of silicon materials, then conventional bonding methods can be used, for example anodic bonding for joining the individual layers. In addition, joining of the carrier layers is also possible by means of gluing techniques. When using plastic materials for the carrier layers, the channel carrier and the channel covering, these can likewise be glued. When using film materials it is again possible to join the various layers to each other as films by lamination, for example by hot lamination or by means of otherwise known sealing methods.

According to the invention, a universal transducer is thus proposed which has a simple construction and enables various measuring methods (amperometry, potentiometry) on the same carrier and with the same measuring solution. This carrier is distinguished by the fact that it is structured in depth. Because of the layer-like structure, in which first of all individual carrier layers are produced, are provided with openings, possibly coated with electrically conductive layers or first coated and then provided with openings and then the individual carrier layers are disposed one above the other and are joined to each other in such a manner that the individual openings produce vertical continuous cavities and then these cavities are filled with suitable fillings, for example substance-detecting membranes or gels, a simple production of three-

dimensionally structured universal transducers of this type according to the invention is possible.

Adhesion agents, for example chrome, can be applied between the carrier layers and the electrically conductive layers. Between the electrically conductive layers and the fillings of the openings there can be introduced further layers, for example anti-interference layers, for example made of cellulose acetate, polyurethane or the like.

BRIEF DESCRIPTION OF THE DRAWINGS (Underline, Letter + Cap)

A few examples of the present universal transducers according to the invention are described subsequently.

There are shown

Fig. 1 a universal transducer with a plurality of sensor elements;

Fig. 2 various glucose sensors;

Fig. 3 various ion-selective electrodes;

Fig. 4 various sensor elements;

Fig. 5 a CO_2 sensor according to the invention;

Fig. 6 an amperometric glucose sensor with flow channel; and

Fig. 7 a universal transducer with a plurality of sensor elements and a flow channel.

DESCRIPTION OF THE PREFERRED EMBODIMENT (with underlining)

In the following embodiments and Figures, the same elements are designated respectively with the same reference numbers. If in one described universal transducer a plurality of sensors (for example I, II, III, IV, V in Fig. 1) are described with the same elements with respect to type or function (for example filling 9) then the reference numbers for these elements which are the same in type or function are assigned to the sensor elements designated respectively with Roman numerals (I - V) by a number after a point (for example 9.1, 9.2, ..., 9.5).

Figure 1 shows a carrier which comprises a first carrier layer 1, a second carrier layer 2 and a third carrier layer 3 which are all joined together securely. These carrier layers 1 to 3 are configured by means of openings 4 to 6 and also by means of electrically conductive layers 7 and 8 such that various sensor elements I to V are produced in the regions of the openings. In the carrier layer 1 there are situated openings 4 (4.1 for the sensor element I, 4.2 for the sensor element II etc.), in the carrier layer 2 there are situated openings 5 (5.1 - 5.5) and in the carrier layer 3 openings 6 (6.1 - 6.5). The openings of the carrier layers 1 to 3 are situated in such a manner one above the other that cavities are produced which extend over the three carrier layers.

An electrically conductive film 7 was applied in part on the surface of the carrier layer 1 and another electrically conductive film 8 on the carrier layer 2. The openings 4 to 6 serve as cavities for receiving fillings 9 (membrane or gel materials). After introduction of the fillings 9, the cavities are sealed by means of an encapsulating material 11. In the opening of the first carrier layer, there is produced one active

sensor surface 10 respectively on the external phase boundary of the filling 9.

A platinum film 7 was produced on the first carrier layer and a silver film on the carrier layer 2 as electrically conductive layers.

On the basis of such a universal transducer, very different sensor elements can be produced.

The element I represents a reference electrode for the other sensor elements. The silver film 8.1 can be chloridated at its interface to the filling 9.1. For example KCl solution in gelatine or in polyvinyl alcohol (PVA) is introduced here from above as a filling 9.1. Such an element corresponds to a conventional Ag/AgCl reference electrode. Such a reference electrode can be used for example together with an ion-selective electrode (ISE).

Such an ion-selective electrode (ISE) is produced as sensor element II. This sensor element II is constructed in the same manner as the element I. However, the cavity here in the region of the openings 4.2, 5.2 and 6.2 is filled with an ion-selective membrane 9.2. This ion-selective membrane is made for example of PVC material or silicone which in addition to a softener and additives also contains an ionophore as an electroactive substance. The PVC membrane 9.2 is in direct contact with the metal film 8.2 (Ag). If a liquid measuring medium interacts with the ion-selective membrane 9.2 in the region of the measuring window 10.2, then a potential difference is formed in the region of the measuring window which can be measured against the reference

electrode I which is itself in contact with the measuring medium in the region of the measuring window 10.1.

The element III shows another potentiometric sensor element which can be used for determining urea. First of all an ion-selective membrane 9.3 for determining ammonium is introduced into the cavity in the region of the openings 5.3 and 6.3 from the direction of the opening 4.3 of the carrier layer 1 or from the opening 6.3 of the carrier layer 3. Such an ion-selective membrane can once again be produced from PVC material with a softener and additives and also with an ionophore for ammonium. Next, a second membrane 9.3.1 is applied to the membrane 9.3 and is made for example of a PCS gel (polycarbamoyl sulfonate) which contains the enzyme urease as biocomponent. During measurement, the liquid measuring medium interacts with the analyte urea in the region of the measuring window 10.3 with the membrane 9.3.1. The urea molecules are converted catalytically by the urease enzyme. The thereby changing ammonium concentration in the membrane 9.3.1 can be detected by means of the ion-selective ammonium membrane 9.3. Measurement is effected against the reference electrode 1. For this purpose, the potential of the urea sensor is measured at the silver film 8.3. The metal film 8.3 extends perpendicularly to the plane of the picture and lies externally freely (12.5) analogously to the metal film 8.5 of the sensor element V. The electrical connection can occur here.

A glucose sensor is produced as sensor element IV. The cavity in the region of the openings 4.4, 5.4 and 6.4 is filled here with PVA which contains the enzyme glucose oxidase (GOD). If glucose from the measuring medium in the region

of the measuring window 10.4 interacts with the membrane material 9.4, then the glucose is converted catalytically by means of the enzyme GOD. H_2O_2 is thereby produced. This H_2O_2 can be electrochemically converted amperometrically on the Pt electrode 7.4. This takes place according to the amperometric measuring principle in which the electrical current is measured between the Pt electrode 7.4 and the Ag/AgCl electrode 8.4. The measurement can be effected in the described manner by means of a two electrode arrangement.

If measurement with potentiometric sensor elements (for example sensor elements II and III) is intended to be effected simultaneously, then it is particularly advantageous because of the configuration of the universal transducer to implement a three electrode measurement in which the potential of the Pt operating electrode 7.4 is determined by means of the reference electrode I. The current of the sensor element IV thereby flows over the Ag/AgCl counter electrode 8.4.

As operating and counter elecrode are disposed according to the invention vertically in a cavity and the reference electrode I comes into contact with the measuring medium above the measuring window 10.1 outwith the cavity of the sensor element IV, the electrical current cannot flow over the measuring window 10.4 and over the measuring medium and hence cannot disturb the measurements at the potentiometric sensor elements.

In an analogous manner to the glucose sensor IV, a sensor element V is produced for determining concentrations of dissolved oxygen in the liquid measuring medium. The cavity

in the region of the openings 4.5, 5.5 and 6.5 is filled here with a KCl solution or a KCl gel. The opening 4.5 in the carrier layer 1 is covered with a gas-permeable membrane 13. The oxygen dissolved in the liquid measuring medium can diffuse through the gas-permeable membrane and is converted electrochemically at the platinum electrode 7.5 according to the amperometric measuring principle. For this purpose, the electrical current between the platinum electrode 7.5 and the Ag/AgCl electrode 8.5 is measured after the application of an electrical voltage of some 100 mV.

Figure 2 a) shows the sensor element IV from Figure 1. Another geometry of the opening 4 in the carrier layer 1 is illustrated in Figure 2 b). Here, the electrically conductive film 7 extends into the region of the opening. This can be achieved in that the film 7 is applied after producing the opening for example by evaporation coating in the vacuum or by sputtering. A similar arrangement is shown in Figure 2 c). Here, the film 7 however does not extend into the region of the internal surface of the opening 4. All three sensor elements are suitable for amperometric measurements. The fillings 9 can contain membrane or gel materials, according respectively to the configuration of the sensor element, and also the most varied biocomponents, as are commonly used here in biosensor analysis. These can be enzymes, micro-organisms or antibodies.

This arrangement of the metal films 7 on the carrier layers 1 makes it possible to produce transducer structures in which the films 7 extend up to the measuring windows 10 or not, according to the configuration of the sensor elements.

In Figure 3, various embodiments of the transducer are illustrated, as are illustrated for ion-selective electrodes according to the example II of Figure 1 or reference electrodes according to the example I of Figure 1. Analogously to the openings in the carrier layer 1 of Figure 2, the openings in this example in the carrier layer 2 are configured differently. Here, the electrically conductive layers 8 extend respectively up to the carrier layer 1 (Fig. 3 a) and b)). In Figure 3 c), the electrically conductive layer 8 is located only on the flat surface of the carrier layer 2.

This arrangement of the metal films 8 on the carrier layers 2 makes it possible to produce transducer structures in which the films 8 have a greater or smaller spacing from the carrier layer 1 and from the measuring window 10 according to the configuration of the sensor element.

If reference electrodes are produced in accordance with the element I of Figure 1, then the electrically conductive layers 8 in Figures 3 a) to c) are made for example of a chloridated silver film. The filling 9 of the cavity in the carrier layers 1 to 3 is made here also of a KCl gel. It is likewise possible to configure ion-selective electrodes with polymer membranes based on the structures according to Figure 3. For this purpose, the electrically conductive layers 8 are produced for example from silver. The fillings 9 of the cavities in the region of the openings 4, 5 and 6 are made in the examples according to Figure 3 a) and b) for example of PVC, silicone or other materials for ion-selective membranes and are provided with the necessary active components.

An ion-selective electrode with an internal electrolyte is illustrated in Figure 3 c). First of all an ion-selective membrane 9.1 is filled from the top into the cavity in the region of the openings 4 and 5. This membrane has itself no contact with an electrically conductive layer. A KCl gel 9 is applied over the ion-selective membrane. This KCl gel 9 is in direct contact with the chloridated silver layer 8.

In the examples according to Figure 4, additional membranes 13 are introduced respectively into the sensor elements. Figure 4 a) shows for example a glucose sensor element which is sealed with a polyurethane (PU) membrane to the measuring window 10. This polyurethane membrane is firmly joined to the carrier layer 1. The electrode layer 14 made of platinum is firmly joined to the membrane 13 and the carrier layer 2. The filling 9 is made here for example of PVA with the enzyme GOD. The filling 9 is in direct contact with a reference electrode layer or a counter electrode layer 8 which is made of a chloridated silver film.

In a similar manner to this glucose sensor according to Figure 4 a), an oxygen sensor element can be produced. Instead of the PU membrane 13 there occurs here a gas-permeable membrane made of for example Teflon or silicone. The filling 9 is made in this case of a KCl solution or a KCl gel.

A further variant of a glucose sensor is illustrated in Figure 4 b). In contrast to Figure 4 a), here the platinum operating electrode 15 is located directly on the carrier layer 1. The membrane 13 is made here likewise of polyurethane.

A further variant of an oxygen sensor is illustrated in Figure 4 c). In contrast to Figure 4 a), the platinum electrode layer 14 is located only under the carrier layer 2.

Based on Figures 4 a) and 4 c), sensors for measuring concentrations of the dissolved carbon dioxide can also be produced in liquid measuring media. Such sensors operate according to the Severinghaus principle. The membrane 13 is made here of gas-permeable material. The filling 9 is an electrolyte gel. The electrode layers 14 are made of iridium oxide which is a pH-sensitive material.

During measurement, the carbon dioxide diffuses through the gas-permeable membrane 13. This changes the pH value in the electrolyte filling 9 which can be measured by means of the pH-sensitive iridium oxide electrode 14 against the reference electrode comprising the chloridated silver film 8.

A CO_2 sensor is illustrated in Figure 5 as a further embodiment. A silver layer 8 and a chloridated silver layer 14 are applied here to the carrier layer 2. After production of the transducer, the cavity in the region of the openings 5 and 6 is filled with a pH-sensitive polymer membrane (for example made of PVC) so that, in conjunction with the silver layer 8, an ion-selective electrode is formed for the pH value. Next, the encapsulation layer 11 is applied. An internal electrolyte 16 is applied to the pH-sensitive membrane and is in contact both with the surface of the pH-sensitive membrane 9 and also with the surface of the chloridated silver layer 14. A gas-permeable membrane 13, which is made for example of silicone, is poured on the internal electrolyte layer 16. The

internal electrolyte also fills the reservoir 16A. This extends the service-life of the sensor.

In this manner, a sensor for measuring CO_2 concentrations in aqueous media is produced according to the Severinghaus principle. During measurement, the carbon dioxide diffuses through the gas-permeable membrane 13. This changes the pH value in the electrolyte layer 16 which can be measured by means of the ion-selective electrode, comprising the ion-selective membrane 9 and the silver layer 8, against the reference electrode which is made of the chloridated silver film 14.

A sensor element according to example IV of Figure 1 is illustrated once again in Figure 6 as a further embodiment. In addition, a flow channel 20 is integrated here. For this purpose, a channel carrier 18 is applied to the carrier layer 1 and contains recesses for the flow channel 20. The channel carrier 18 is closed by means of a channel covering 19. In this manner, flow channels 20 can be produced with very small cross-sections. It is likewise possible to connect various sensor elements (such as are illustrated for example in Figure 1) with the same channel.

In analogy to and extension of Figure 6, an embodiment is illustrated in Figure 7 with a through-flow channel 20. This example was derived from Figure 1. Instead of the sensor elements I and V, there are located here now the connections 21 and 22 for the supply and discharge of the liquid measuring medium. The liquid measuring medium enters into the channel 20 which comprises the channel carrier 18 and the covering 19. In this example, the element II can be a

reference electrode with a chloridated silver electrode 8.2 which contains a filling 9.2 made of a KCl gel. The sensor element at the position III is, as in the example according to Figure 1, a urea sensor, while at position IV a glucose sensor is situated. The urea sensor III is measured against the reference electrode II according to the potentiometric measuring method. The glucose sensor IV is measured according to the three electrode principle. For this purpose, the platinum electrode 7.4 is used as operating electrode. The silver film 8.4 serves as a counter electrode which can be subject to a current while the reference electrode II serves for adjusting the polarisation voltage of the operating electrode 7.4.

Patent Claims

1. Universal transducer for chemo- and/or biosensor analysis for determining substance concentrations or substance activities in fluids having

   - a carrier comprising a first (1) and a second (2) flat carrier layer,
   - at least one opening (4.1 - 4.5, 5.1 - 5.5) respectively in each of the two carrier layers (1, 2),
   - at least one continuous cavity which is formed respectively by one opening (4, 5) in each of the two carrier layers and extends from a first active surface of the carrier over the first and second carrier layer (1, 2),
   - a filling (9) which is disposed in the cavity and is contactable with the analyte in the region of a first active surface (10) of the carrier, and
   - at least one electrically conductive layer (8) which is disposed at least in part on the surface of one of the two carrier layers (1, 2), which surface is orientated away from the first active surface (10), in contact with the filling (9).

2. Universal transducer according to the preceding claim, characterised in that the carrier has further flat carrier layers (3).

3. Universal transducer according to the preceding claim, characterised in that the further flat carrier layers (3) have at least in part further openings (6.1 - 6.5) which are continuous with at least one of the hollow spaces.

4. Universal transducer according to the preceding claim,

characterised in that fillings (9) are disposed in the further openings (6.1 - 6.5).

5. Universal transducer according to one of the preceding claims, characterised in that the filling (9) or fillings contain a substance-detecting membrane and/or gel.

6. Universal transducer according to one of the preceding claims, characterised in that there is disposed on the surface of the first (1), the second (2) and/or the further (3) carrier layers, which are orientated away from the first active surface (10), at least in part at least one electrically conductive layer (7, 8) respectively.

7. Universal transducer according to one of the preceding claims, characterised in that at least one of the openings (4) is configured so as to taper conically towards the frst active surface (10).

8. Universal transducer according to one of the preceding claims, characterised in that the electrically conductive layer (7, 8) extends at least in part towards the lateral walls of the adjacent opening (4, 5).

9. Universal transducer according to one of the preceding claims, characterised in that the first active surface (10) in the region of the opening in the carrier layer (1) adjacent to the first active surface (10) is covered with a further membrane (13), for example with a gas-permeable membrane.

10. Universal transducer according to the preceding claim, characterised in that the further membrane (13) has a thickness of 1 µm up to a few µm.

11. Universal transducer according to one of the two preceding claims, characterised in that the further membrane (13) contains polyvinyl chloride (PVC), polyethylene (PE), polyoxymethylene (POM), polycarbonate (PC), ethylene/propylene-Cop (EPDM), polyvinylidene chloride (PVDC), polyvinyl butyral (PVB), cellulose acetate (CA), polypropylene (PP), polymethylmethacrylate (PMMA), polyamide (PA), tetrafluoroethylene/hexafluoropropylene-Cop (FEP), polytetrafluoroethylene (PTFE), phenol formaldehyde (PF), epoxide (EP), polyurethane (PUR), polyester (UP), silicone, melamine formaldehyde (MF), urea formaldehyde (UF), aniline formaldehyde or capton.

12. Universal transducer according to one of the three preceding claims, characterised in that an electrically conductive layer (14) is disposed between the first active surface (10) and the second membrane (13).

13. Universal transducer according to one of the preceding claims, characterised in that the cavity on its surface, which is orientated away from the first active surface (10), is covered with an encapsulation (11).

14. Universal transducer according to the preceding claim, characterised in that the encapsulation (11) is made of an epoxide resin.

15. Universal transducer according to one of the preceding claims, characterised in that the openings contain at least in part different fillings (9, 9.3, 9.31).

16. Universal transducer according to one of the preceding claims, characterised in that a channel carrier (18) with a flow channel (20) and a channel covering (19) thereon are disposed on the first active

surface (10) in such a manner that the flow channel (20) is in contact with at least one opening (4.1 - 4.3) in the carrier layer (1) in the region of the first active surface (10).

17. Universal transducer according to the preceding claim, characterised in that the thickness of the channel carrier (18) and/or of the channel covering (19) is a few µm up to a few mm, preferably some 100 µm.

18. Universal transducer according to one of the preceding claims, characterised in that at least one of the carrier layers (1, 2, 3) contains plastic materials such as polyvinyl chloride (PVC), polyethylene (PE), polyoxymethylene (POM), polycarbonate (PC), ethylene/propylene-Cop (EPDM), polyvinylidene chloride (PVDC), polychlorotrifluorethylene, polyvinyl butyral (PVB), cellulose acetate (CA), polypropylene (PP), polymethylmethacrylate (PMMA), polyamide (PA), tetrafluoroethylene/hexafluoropropylene-Cop (FEP), polytetrafluoroethylene (PTFE), phenol formaldehyde (PF), epoxide (EP), polyurethane (PUR), polyester (UP), silicone, melamine formaldehyde (MF), urea formaldehyde (UF), aniline formaldehyde, capton or others or silicon, ceramic or glass.

19. Universal transducer according to one of the preceding claims, characterised in that the thickness of at least one of the carrier layers (1, 2, 3) is between some few µm up to a few mm, preferably some 100 µm.

20. Universal transducer according to one of the preceding claims, characterised in that at least one of the electrically conductive layers (7, 8) is made of metals, especially noble metals such as platinum,

gold and silver or metal alloys or screen printing pastes, for example based on graphite or metallic materials.

21. Universal transducer according to one of the preceding claims, characterised in that the thickness of at least one of the electrically conductive layers (7, 8) is 1 µm up to some µm.

22. Universal transducer according to one of the preceding claims, characterised in that the filling (9) as a membrane contains PVC, silicone, polyurethane and the like and/or as a gel (9), gelatine or polyvinyl alcohol (PVA) or the like.

23. Universal transducer according to one of the preceding claims, characterised in that the filling contains biocomponents such as enzymes, micro-organisms and/or antibodies.

24. Universal transducer according to one of the preceding claims, characterised in that the diameter of at least one of the openings (4.1 - 4.5) of the carrier layer (1) adjacent to the first active surface (10) on the first active surface (10) is a few µm up to a few mm, preferably some 10 - 100 µm.

25. Universal transducer according to one of the preceding claims, characterised in that the carrier has two cavities (4.2, 5.2, 6.2 and 4.4, 5.4, 6.4), a filling being disposed in each of the cavities, the filling of the one cavity being in contact with a first electrically conductive layer as reference electrode and the filling of the second cavity being in contact with second or third conductive layers, which are disposed on different carrier layers, as the operating electrode or counter electrode which are subject to a current, and the first,

second and third conductive layer forming a three electrode arrangement for amperometric measurements.

26. Universal transducer according to the preceding claim, characterised in that the carrier has a third cavity, in which a filling is disposed which is in contact with a further electrically conductive layer which forms a potentiometric electrode and is measurable against the reference electrode.

27. Use of universal transducers according to at least one of the preceding claims as reference electrode, as sensor element for potentiometric determination and/or as sensor element for amperometric determination of analyte concentrations or ion activities.

28. Use according to the preceding claim for determining the concentration of dissolved carbon dioxide, oxygen, glucose and/or other metabolites and/or urea or for determining the pH value or other parameters.

Abstract

The present application relates to a universal transducer and chemo- and biosensors based on miniaturised universal transducers of this type which are used for example in chemical analysis, medicinal diagnosis and the like for determining substance concentrations or ion activities in fluids.

The universal transducer according to the invention has a carrier which comprises at least two flat carrier layers (1, 2), each of the two carrier layers (1, 2) having at least one opening (4, 5). These openings (4, 5) form a continuous cavity which extends from a first active surface of the carrier over the first and the second carrier layer (1, 2). On the surfaces of at least one of the two carrier layers (1, 2), which surfaces are orientated away from the first active surface (10), there is disposed at least in part one electrically conductive layer which is in contact with a filling of the cavity.

(Figure 2c)

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Universal transducer

The present invention relates to a universal transducer and also chemo- and biosensors based on miniaturised universal transducers of this type. Sensors of this type are used for example in chemical analysis or in medical diagnosis for determining substance concentrations or ion activities in fluids.

According to the state of the art, chemo- and biosensor elements are produced based on carriers with metal contacts and membrane or gel materials which are specific for the respective analyte. On ion-selective electrodes, potential differences are thereby measured according to the potentiometric measuring principle against a reference electrode. In amperometric sensors, currents between

operating and reference electrodes or counter electrodes are determined after application of an electrical voltage according to the two electrode or three electrode principle (see Friedrich Oehme, Chemical Sensors, Vieweg Press 1991).

P 41 15 414 discloses chemo- and biosensors of this type which are extremely miniaturised. Cavities are thereby integrated in carriers made of semiconductor materials such as silicon, said cavities being covered with a metal film on their internal surface and containing the respective substance-detecting membrane- or gel materials.

It is however disadvantageous in the state of the art that the carriers for such sensors can only be provided with two different metal films, for example for amperometric measurements, if these metal films are structured photolithographically in depth on the three-dimensional surface of the cavities. Even when the electrically conductive film is not allowed to come into direct contact with the measuring medium, the internal surface of the cavity in the contact region must be structured photolithographically with the measuring medium in order not to apply any metal film in this contact region. Three-dimensionally photolithographic structuring methods of this type imply however a significant technological complexity and cost.

A further disadvantage of this state of the art is that, with the sensor elements disclosed there, it has not been possible to date to operate amperometric and potentiometric sensor elements together on only one single carrier. For, in the case of the state of the art, both the amperometric and also the potentiometric sensor elements are in contact with the same

measuring medium and the electrical currents of the amperometric sensors flow over the interface between the membrane and the measuring medium. The potential measurements of the adjacent potentiometric sensors are thereby disturbed.

It is therefore the object of the present invention to make available a universal transducer which is simple to produce and which permits a three-dimensional structuring of the transducer by simple means. These universal transducers should furthermore be suitable in order to use amperometric and potentiometric sensors for determining the same fluid at the same time.

This object is achieved by the universal transducer according to claim 1 and also its usages according to claim 27. Advantageous developments of the universal transducer according to the invention and of uses according to the invention are given in the dependent claims.

According to the invention, the universal transducer has a carrier which comprises at least two flat carrier layers. A cavity extends by means of openings through these carrier layers and can be contacted on one side of the carrier with the analyte. The sides of the carrier layers which are orientated away from this contact surface are provided with electrically conductive layers or films as electrodes. The cavity itself is filled with a filling which can contain a substance-detecting membrane and/or gel, for example an ion-selective membrane. According to the invention, it is therefore possible with such a structure to build up the individual carrier layers and electrodes successively, as a

result of which a three-dimensional photolithographical structuring can be dispensed with. Therefore a transducer can be produced for example without special photolithographic structuring, the electrodes of said transducer not coming into contact with the measuring medium. If the transducer has only one electrically conductive layer, then this can be disposed on one of the carrier layers which is further away from the first active surface, while the carrier layer which forms the first active surface has no electrically conductive layer. As a result, a contact between the electrically conductive layer and the measuring medium can be avoided in a simple manner. In total, it is possible to dispose the electrodes, in contrast to the state of the art, three-dimensionally in the direction of the depth of the universal transducer. Furthermore, it is also possible to provide a plurality of such cavities as universal transducers on the same carrier in order to produce for example a plurality of amperometric or a plurality of potentiometric sensors or even amperometric and potentiometric sensors for the same measuring medium at the same time on the same carrier.

The difference between potentiometric and amperometric sensor elements lies thereby simply in the locally selective application of the electrode layers, for example by sputtering with the help of shadow masks.

In particular, the structure of the amperometric and potentiometric sensors for the most varied of analytes is effected according to a uniform principle, very different sensor elements being able to be produced however simultaneously. The carrier layers for different sensor elements differ thereby

possibly only by the configuration of the openings in the individual carrier layers. As the electrode layers and also the fillings can be applied in a locally selective manner, for example via the insertion of different substance-detecting materials in the cavities in the region of the respective openings, a vertical structure of the individual sensor systems is possible.

In this way, universal transducers can therefore also be produced, the further formation of which into multi-sensors with different sensor element types can also be decided later.

The carrier layers of the universal transducer according to the invention are advantageously made of plastic materials such as polyvinyl fluoride, polyethylene, polyoxymethylene, polycarbonate, ethylene/propylene-COP, polyvinylidene chloride, polychlorotrifluoroethylene, polyvinyl butyral, cellulose acetate, polypropylene, polymethylmethacrylate, polyamide, tetrafluoroethylene/hexafluoropropylene-COP, polytetrafluoroethylene, phenol formaldehyde, epoxide, polyurethane, polyester, silicone, melamine formaldehyde, urea formaldehyde, aniline formaldehyde, capton or the like or also made of silicon, ceramic or glass. The universal transducer according to the invention can hence be produced based on different production technologies, such as plastic material injection moulding technology, plastic material film technology, ceramics technology or even silicon technology.

The electrically conductive layers can comprise metals, in particular noble metals such as platinum, gold or silver or even metal alloys or screen printing pastes, for example based on graphite or metallic materials.

The fillings are produced advantageously from materials which are known conventionally for ion-selective membranes, such as for example, PVC, silicone, polyurethane or the like. For the gel fillings there are used for example gelatine or polyvinyl alcohol or the like.

The encapsulation can advantageously comprise materials which are compatible with the materials of the membranes or gels, for example epoxide resins.

For the further membrane, which covers the measuring window of a diameter in the region of a first active surface, for example a gas-permeable membrane, very thin materials are used preferably, in the range of 1 µm up to a few micrometers, advantageously the materials polyvinyl fluoride, polyethylene, polyoxymethylene, polycarbonate, ethylene/propylene-COP, polyvinylidene chloride, polychlorotrifluoroethylene, polyvinyl butyral, cellulose acetate, polypropylene, polymethylmethacrylate, polyamide, tetrafluoroethylene/hexafluoropropylene-COP, polytetrafluoroethylene, phenol formaldehyde, epoxide, polyurethane, polyester, silicone, melamine formaldehyde, urea formaldehyde, silicone, aniline formaldehyde, capton or the like. These further membranes are glued advantageously on the first active surface of the first carrier layer or are poured from the liquid phase.

The thicknesses of the individual carrier layers can be between a few µm up to a few mm, preferably in the range of less than 100 µm. The apertures of the openings (measuring

windows) in the first carrier layer in the region of the first active surface are likewise advantageously in the range of a few µm to a few mm, preferably some 10 to 100 µm. The thicknesses of the electrically conductive layers which are applied as electrodes on the surfaces of the individual carrier layers, which surfaces are orientated away from the first active surface, are in the range of a few µm.

The flow channels provided in an advantageous embodiment forming channel carriers and channel coverings, which bring the liquid with the analyte to the individual measuring windows, comprise advantageously the same materials as the individual carrier layers. The channel carrier and the channel covering have thereby thicknesses of a few µm to a few mm, preferably some 100 µm.

According to the respective choice of material, the shaping of the carrier layers is effected by different methods. If the carrier layers are made for example of silicon, then the production of the openings can be effected by the method of deep etching. Etching media such as KOH or dry etching methods are used hereby for example. Openings are thereby produced which can have different cross-sections, for example square, rectangular or round. In the case of anisotropic etching, openings are produced thereby in the shape of a truncated pyramid which taper from one side of the carrier layer to the other side of the carrier layer, for example in the direction of the first active surface.

When using plastic materials for the carrier layers, these can be produced by injection moulding. The openings are hereby

caused by the shaping of the injection moulding tool. However it is also possible to use flat carrier materials, for example plastic material films for the individual carrier layers, which are then provided with openings by cutting, boring, micro-imprinting or etching methods. Advantageously, laser cutting can also be used.

The electrically conductive layers are applied on the carrier layers with known methods of thin layer technology by evaporation coating in the vacuum or by sputtering. The structuring can thereby occur in that evaporation coating or sputtering is produced by shadow masks. In addition, the use of photolithography is nevertheless possible, however for producing the transducers according to the invention there being no need for structuring in depth in a three-dimensional manner at all. It is likewise possible to produce the electrically conductive electrodes by means of the screen printing method or by electrolytic deposition.

The fillings of the openings, for example made of membranes or gels, are advantageously introduced into the cavities by means of an automatic dispensing device. This method is also suitable for applying the encapsulation, which however can also be applied with the screen printing method.

In order to produce the transducers according to the invention, first of all the carrier layers are provided with openings and then electrically conductive layers are applied if necessary individually respectively. The electrically conductive layers can also be applied before the production of the openings.

Then the carrier layers and possibly the channel carrier and the channel covering are placed one above the other and joined to each other. For the purpose of joining, various materials and methods are used according respectively to the material of the carrier layers and of the channel carrier or the channel covering. If the carrier layers and the channel carrier/channel covering are made of silicon materials, then conventional bonding methods can be used, for example anodic bonding for joining the individual layers. In addition, joining of the carrier layers is also possible by means of gluing techniques. When using plastic materials for the carrier layers, the channel carrier and the channel covering, these can likewise be glued. When using film materials it is again possible to join the various layers to each other as films by lamination, for example by hot lamination or by means of otherwise known sealing methods.

According to the invention, a universal transducer is thus proposed which has a simple construction and enables various measuring methods (amperometry, potentiometry) on the same carrier and with the same measuring solution. This carrier is distinguished by the fact that it is structured in depth. Because of the layer-like structure, in which first of all individual carrier layers are produced, are provided with openings, possibly coated with electrically conductive layers or first coated and then provided with openings and then the individual carrier layers are disposed one above the other and are joined to each other in such a manner that the individual openings produce vertical continuous cavities and then these cavities are filled with suitable fillings, for example substance-detecting membranes or gels, a simple production of three-

dimensionally structured universal transducers of this type according to the invention is possible.

Adhesion agents, for example chrome, can be applied between the carrier layers and the electrically conductive layers. Between the electrically conductive layers and the fillings of the openings there can be introduced further layers, for example anti-interference layers, for example made of cellulose acetate, polyurethane or the like.

A few examples of the present universal transducers according to the invention are described subsequently.

There are shown

Fig. 1 a universal transducer with a plurality of sensor elements;

Fig. 2 various glucose sensors;

Fig. 3 various ion-selective electrodes;

Fig. 4 various sensor elements;

Fig. 5 a CO_2 sensor according to the invention;

Fig. 6 an amperometric glucose sensor with flow channel; and

Fig. 7 a universal transducer with a plurality of sensor elements and a flow channel.

In the following embodiments and Figures, the same elements are designated respectively with the same reference numbers. If in one described universal transducer a plurality of sensors (for example I, II, III, IV, V in Fig. 1) are described with the same elements with respect to type or function (for example filling 9) then the reference numbers for these elements which are the same in type or function are assigned to the sensor elements designated respectively with Roman numerals (I - V) by a number after a point (for example 9.1, 9.2, ..., 9.5).

Figure 1 shows a carrier which comprises a first carrier layer 1, a second carrier layer 2 and a third carrier layer 3 which are all joined together securely. These carrier layers 1 to 3 are configured by means of openings 4 to 6 and also by means of electrically conductive layers 7 and 8 such that various sensor elements I to V are produced in the regions of the openings. In the carrier layer 1 there are situated openings 4 (4.1 for the sensor element I, 4.2 for the sensor element II etc.), in the carrier layer 2 there are situated openings 5 (5.1 - 5.5) and in the carrier layer 3 openings 6 (6.1 - 6.5). The openings of the carrier layers 1 to 3 are situated in such a manner one above the other that cavities are produced which extend over the three carrier layers.

An electrically conductive film 7 was applied in part on the surface of the carrier layer 1 and another electrically conductive film 8 on the carrier layer 2. The openings 4 to 6 serve as cavities for receiving fillings 9 (membrane or gel materials). After introduction of the fillings 9, the cavities are sealed by means of an encapsulating material 11. In the opening of the first carrier layer, there is produced one active

sensor surface 10 respectively on the external phase boundary of the filling 9.

A platinum film 7 was produced on the first carrier layer and a silver film on the carrier layer 2 as electrically conductive layers.

On the basis of such a universal transducer, very different sensor elements can be produced.

The element I represents a reference electrode for the other sensor elements. The silver film 8.1 can be chloridated at its interface to the filling 9.1. For example KCl solution in gelatine or in polyvinyl alcohol (PVA) is introduced here from above as a filling 9.1. Such an element corresponds to a conventional Ag/AgCl reference electrode. Such a reference electrode can be used for example together with an ion-selective electrode (ISE).

Such an ion-selective electrode (ISE) is produced as sensor element II. This sensor element II is constructed in the same manner as the element I. However, the cavity here in the region of the openings 4.2, 5.2 and 6.2 is filled with an ion-selective membrane 9.2. This ion-selective membrane is made for example of PVC material or silicone which in addition to a softener and additives also contains an ionophore as an electroactive substance. The PVC membrane 9.2 is in direct contact with the metal film 8.2 (Ag). If a liquid measuring medium interacts with the ion-selective membrane 9.2 in the region of the measuring window 10.2, then a potential difference is formed in the region of the measuring window which can be measured against the reference

electrode I which is itself in contact with the measuring medium in the region of the measuring window 10.1.

The element III shows another potentiometric sensor element which can be used for determining urea. First of all an ion-selective membrane 9.3 for determining ammonium is introduced into the cavity in the region of the openings 5.3 and 6.3 from the direction of the opening 4.3 of the carrier layer 1 or from the opening 6.3 of the carrier layer 3. Such an ion-selective membrane can once again be produced from PVC material with a softener and additives and also with an ionophore for ammonium. Next, a second membrane 9.3.1 is applied to the membrane 9.3 and is made for example of a PCS gel (polycarbamoyl sulfonate) which contains the enzyme urease as biocomponent. During measurement, the liquid measuring medium interacts with the analyte urea in the region of the measuring window 10.3 with the membrane 9.3.1. The urea molecules are converted catalytically by the urease enzyme. The thereby changing ammonium concentration in the membrane 9.3.1 can be detected by means of the ion-selective ammonium membrane 9.3. Measurement is effected against the reference electrode 1. For this purpose, the potential of the urea sensor is measured at the silver film 8.3. The metal film 8.3 extends perpendicularly to the plane of the picture and lies externally freely (12.5) analogously to the metal film 8.5 of the sensor element V. The electrical connection can occur here.

A glucose sensor is produced as sensor element IV. The cavity in the region of the openings 4.4, 5.4 and 6.4 is filled here with PVA which contains the enzyme glucose oxidase (GOD). If glucose from the measuring medium in the region

of the measuring window 10.4 interacts with the membrane material 9.4, then the glucose is converted catalytically by means of the enzyme GOD. H_2O_2 is thereby produced. This H_2O_2 can be electrochemically converted amperometrically on the Pt electrode 7.4. This takes place according to the amperometric measuring principle in which the electrical current is measured between the Pt electrode 7.4 and the Ag/AgCl electrode 8.4. The measurement can be effected in the described manner by means of a two electrode arrangement.

If measurement with potentiometric sensor elements (for example sensor elements II and III) is intended to be effected simultaneously, then it is particularly advantageous because of the configuration of the universal transducer to implement a three electrode measurement in which the potential of the Pt operating electrode 7.4 is determined by means of the reference electrode I. The current of the sensor element IV thereby flows over the Ag/AgCl counter electrode 8.4.

As operating and counter elecrode are disposed according to the invention vertically in a cavity and the reference electrode I comes into contact with the measuring medium above the measuring window 10.1 outwith the cavity of the sensor element IV, the electrical current cannot flow over the measuring window 10.4 and over the measuring medium and hence cannot disturb the measurements at the potentiometric sensor elements.

In an analogous manner to the glucose sensor IV, a sensor element V is produced for determining concentrations of dissolved oxygen in the liquid measuring medium. The cavity

in the region of the openings 4.5, 5.5 and 6.5 is filled here with a KCl solution or a KCl gel. The opening 4.5 in the carrier layer 1 is covered with a gas-permeable membrane 13. The oxygen dissolved in the liquid measuring medium can diffuse through the gas-permeable membrane and is converted electrochemically at the platinum electrode 7.5 according to the amperometric measuring principle. For this purpose, the electrical current between the platinum electrode 7.5 and the Ag/AgCl electrode 8.5 is measured after the application of an electrical voltage of some 100 mV.

Figure 2 a) shows the sensor element IV from Figure 1. Another geometry of the opening 4 in the carrier layer 1 is illustrated in Figure 2 b). Here, the electrically conductive film 7 extends into the region of the opening. This can be achieved in that the film 7 is applied after producing the opening for example by evaporation coating in the vacuum or by sputtering. A similar arrangement is shown in Figure 2 c). Here, the film 7 however does not extend into the region of the internal surface of the opening 4. All three sensor elements are suitable for amperometric measurements. The fillings 9 can contain membrane or gel materials, according respectively to the configuration of the sensor element, and also the most varied biocomponents, as are commonly used here in biosensor analysis. These can be enzymes, micro-organisms or antibodies.

This arrangement of the metal films 7 on the carrier layers 1 makes it possible to produce transducer structures in which the films 7 extend up to the measuring windows 10 or not, according to the configuration of the sensor elements.

In Figure 3, various embodiments of the transducer are illustrated, as are illustrated for ion-selective electrodes according to the example II of Figure 1 or reference electrodes according to the example I of Figure 1. Analogously to the openings in the carrier layer 1 of Figure 2, the openings in this example in the carrier layer 2 are configured differently. Here, the electrically conductive layers 8 extend respectively up to the carrier layer 1 (Fig. 3 a) and b)). In Figure 3 c), the electrically conductive layer 8 is located only on the flat surface of the carrier layer 2.

This arrangement of the metal films 8 on the carrier layers 2 makes it possible to produce transducer structures in which the films 8 have a greater or smaller spacing from the carrier layer 1 and from the measuring window 10 according to the configuration of the sensor element.

If reference electrodes are produced in accordance with the element I of Figure 1, then the electrically conductive layers 8 in Figures 3 a) to c) are made for example of a chloridated silver film. The filling 9 of the cavity in the carrier layers 1 to 3 is made here also of a KCl gel. It is likewise possible to configure ion-selective electrodes with polymer membranes based on the structures according to Figure 3. For this purpose, the electrically conductive layers 8 are produced for example from silver. The fillings 9 of the cavities in the region of the openings 4, 5 and 6 are made in the examples according to Figure 3 a) and b) for example of PVC, silicone or other materials for ion-selective membranes and are provided with the necessary active components.

An ion-selective electrode with an internal electrolyte is illustrated in Figure 3 c). First of all an ion-selective membrane 9.1 is filled from the top into the cavity in the region of the openings 4 and 5. This membrane has itself no contact with an electrically conductive layer. A KCl gel 9 is applied over the ion-selective membrane. This KCl gel 9 is in direct contact with the chloridated silver layer 8.

In the examples according to Figure 4, additional membranes 13 are introduced respectively into the sensor elements. Figure 4 a) shows for example a glucose sensor element which is sealed with a polyurethane (PU) membrane to the measuring window 10. This polyurethane membrane is firmly joined to the carrier layer 1. The electrode layer 14 made of platinum is firmly joined to the membrane 13 and the carrier layer 2. The filling 9 is made here for example of PVA with the enzyme GOD. The filling 9 is in direct contact with a reference electrode layer or a counter electrode layer 8 which is made of a chloridated silver film.

In a similar manner to this glucose sensor according to Figure 4 a), an oxygen sensor element can be produced. Instead of the PU membrane 13 there occurs here a gas-permeable membrane made of for example Teflon or silicone. The filling 9 is made in this case of a KCl solution or a KCl gel.

A further variant of a glucose sensor is illustrated in Figure 4 b). In contrast to Figure 4 a), here the platinum operating electrode 15 is located directly on the carrier layer 1. The membrane 13 is made here likewise of polyurethane.

A further variant of an oxygen sensor is illustrated in Figure 4 c). In contrast to Figure 4 a), the platinum electrode layer 14 is located only under the carrier layer 2.

Based on Figures 4 a) and 4 c), sensors for measuring concentrations of the dissolved carbon dioxide can also be produced in liquid measuring media. Such sensors operate according to the Severinghaus principle. The membrane 13 is made here of gas-permeable material. The filling 9 is an electrolyte gel. The electrode layers 14 are made of iridium oxide which is a pH-sensitive material.

During measurement, the carbon dioxide diffuses through the gas-permeable membrane 13. This changes the pH value in the electrolyte filling 9 which can be measured by means of the pH-sensitive iridium oxide electrode 14 against the reference electrode comprising the chloridated silver film 8.

A CO_2 sensor is illustrated in Figure 5 as a further embodiment. A silver layer 8 and a chloridated silver layer 14 are applied here to the carrier layer 2. After production of the transducer, the cavity in the region of the openings 5 and 6 is filled with a pH-sensitive polymer membrane (for example made of PVC) so that, in conjunction with the silver layer 8, an ion-selective electrode is formed for the pH value. Next, the encapsulation layer 11 is applied. An internal electrolyte 16 is applied to the pH-sensitive membrane and is in contact both with the surface of the pH-sensitive membrane 9 and also with the surface of the chloridated silver layer 14. A gas-permeable membrane 13, which is made for example of silicone, is poured on the internal electrolyte layer 16. The

internal electrolyte also fills the reservoir 16A. This extends the service-life of the sensor.

In this manner, a sensor for measuring CO_2 concentrations in aqueous media is produced according to the Severinghaus principle. During measurement, the carbon dioxide diffuses through the gas-permeable membrane 13. This changes the pH value in the electrolyte layer 16 which can be measured by means of the ion-selective electrode, comprising the ion-selective membrane 9 and the silver layer 8, against the reference electrode which is made of the chloridated silver film 14.

A sensor element according to example IV of Figure 1 is illustrated once again in Figure 6 as a further embodiment. In addition, a flow channel 20 is integrated here. For this purpose, a channel carrier 18 is applied to the carrier layer 1 and contains recesses for the flow channel 20. The channel carrier 18 is closed by means of a channel covering 19. In this manner, flow channels 20 can be produced with very small cross-sections. It is likewise possible to connect various sensor elements (such as are illustrated for example in Figure 1) with the same channel.

In analogy to and extension of Figure 6, an embodiment is illustrated in Figure 7 with a through-flow channel 20. This example was derived from Figure 1. Instead of the sensor elements I and V, there are located here now the connections 21 and 22 for the supply and discharge of the liquid measuring medium. The liquid measuring medium enters into the channel 20 which comprises the channel carrier 18 and the covering 19. In this example, the element II can be a

reference electrode with a chloridated silver electrode 8.2 which contains a filling 9.2 made of a KCl gel. The sensor element at the position III is, as in the example according to Figure 1, a urea sensor, while at position IV a glucose sensor is situated. The urea sensor III is measured against the reference electrode II according to the potentiometric measuring method. The glucose sensor IV is measured according to the three electrode principle. For this purpose, the platinum electrode 7.4 is used as operating electrode. The silver film 8.4 serves as a counter electrode which can be subject to a current while the reference electrode II serves for adjusting the polarisation voltage of the operating electrode 7.4.

Patent Claims

1. Universal transducer for chemo- and/or biosensor analysis for determining substance concentrations or substance activities in fluids having

    - a carrier comprising a first (1) and a second (2) flat carrier layer,
    - at least one opening (4.1 - 4.5, 5.1 - 5.5) respectively in each of the two carrier layers (1, 2),
    - at least one continuous cavity which is formed respectively by one opening (4, 5) in each of the two carrier layers and extends from a first active surface of the carrier over the first and second carrier layer (1, 2),
    - a filling (9) which is disposed in the cavity and is contactable with the analyte in the region of a first active surface (10) of the carrier, and
    - at least one electrically conductive layer (8) which is disposed at least in part on the surface of one of the two carrier layers (1, 2), which surface is orientated away from the first active surface (10), in contact with the filling (9).

2. Universal transducer according to the preceding claim, characterised in that the carrier has further flat carrier layers (3).

3. Universal transducer according to the preceding claim, characterised in that the further flat carrier layers (3) have at least in part further openings (6.1 - 6.5) which are continuous with at least one of the hollow spaces.

4. Universal transducer according to the preceding claim,

characterised in that fillings (9) are disposed in the further openings (6.1 - 6.5).

5. Universal transducer according to one of the preceding claims, characterised in that the filling (9) or fillings contain a substance-detecting membrane and/or gel.

6. Universal transducer according to one of the preceding claims, characterised in that there is disposed on the surface of the first (1), the second (2) and/or the further (3) carrier layers, which are orientated away from the first active surface (10), at least in part at least one electrically conductive layer (7, 8) respectively.

7. Universal transducer according to one of the preceding claims, characterised in that at least one of the openings (4) is configured so as to taper conically towards the frst active surface (10).

8. Universal transducer according to one of the preceding claims, characterised in that the electrically conductive layer (7, 8) extends at least in part towards the lateral walls of the adjacent opening (4, 5).

9. Universal transducer according to one of the preceding claims, characterised in that the first active surface (10) in the region of the opening in the carrier layer (1) adjacent to the first active surface (10) is covered with a further membrane (13), for example with a gas-permeable membrane.

10. Universal transducer according to the preceding claim, characterised in that the further membrane (13) has a thickness of 1 μm up to a few μm.

11. Universal transducer according to one of the two preceding claims, characterised in that the further membrane (13) contains polyvinyl chloride (PVC), polyethylene (PE), polyoxymethylene (POM), polycarbonate (PC), ethylene/propylene-Cop (EPDM), polyvinylidene chloride (PVDC), polyvinyl butyral (PVB), cellulose acetate (CA), polypropylene (PP), polymethylmethacrylate (PMMA), polyamide (PA), tetrafluoroethylene/hexafluoropropylene-Cop (FEP), polytetrafluoroethylene (PTFE), phenol formaldehyde (PF), epoxide (EP), polyurethane (PUR), polyester (UP), silicone, melamine formaldehyde (MF), urea formaldehyde (UF), aniline formaldehyde or capton.

12. Universal transducer according to one of the three preceding claims, characterised in that an electrically conductive layer (14) is disposed between the first active surface (10) and the second membrane (13).

13. Universal transducer according to one of the preceding claims, characterised in that the cavity on its surface, which is orientated away from the first active surface (10), is covered with an encapsulation (11).

14. Universal transducer according to the preceding claim, characterised in that the encapsulation (11) is made of an epoxide resin.

15. Universal transducer according to one of the preceding claims, characterised in that the openings contain at least in part different fillings (9, 9.3, 9.31).

16. Universal transducer according to one of the preceding claims, characterised in that a channel carrier (18) with a flow channel (20) and a channel covering (19) thereon are disposed on the first active

surface (10) in such a manner that the flow channel (20) is in contact with at least one opening (4.1 - 4.3) in the carrier layer (1) in the region of the first active surface (10).

17. Universal transducer according to the preceding claim, characterised in that the thickness of the channel carrier (18) and/or of the channel covering (19) is a few μm up to a few mm, preferably some 100 μm.

18. Universal transducer according to one of the preceding claims, characterised in that at least one of the carrier layers (1, 2, 3) contains plastic materials such as polyvinyl chloride (PVC), polyethylene (PE), polyoxymethylene (POM), polycarbonate (PC), ethylene/propylene-Cop (EPDM), polyvinylidene chloride (PVDC), polychlorotrifluorethylene, polyvinyl butyral (PVB), cellulose acetate (CA), polypropylene (PP), polymethylmethacrylate (PMMA), polyamide (PA), tetrafluoroethylene/hexafluoropropylene-Cop (FEP), polytetrafluoroethylene (PTFE), phenol formaldehyde (PF), epoxide (EP), polyurethane (PUR), polyester (UP), silicone, melamine formaldehyde (MF), urea formaldehyde (UF), aniline formaldehyde, capton or others or silicon, ceramic or glass.

19. Universal transducer according to one of the preceding claims, characterised in that the thickness of at least one of the carrier layers (1, 2, 3) is between some few μm up to a few mm, preferably some 100 μm.

20. Universal transducer according to one of the preceding claims, characterised in that at least one of the electrically conductive layers (7, 8) is made of metals, especially noble metals such as platinum,

gold and silver or metal alloys or screen printing pastes, for example based on graphite or metallic materials.

21. Universal transducer according to one of the preceding claims, characterised in that the thickness of at least one of the electrically conductive layers (7, 8) is 1 µm up to some µm.

22. Universal transducer according to one of the preceding claims, characterised in that the filling (9) as a membrane contains PVC, silicone, polyurethane and the like and/or as a gel (9), gelatine or polyvinyl alcohol (PVA) or the like.

23. Universal transducer according to one of the preceding claims, characterised in that the filling contains biocomponents such as enzymes, micro-organisms and/or antibodies.

24. Universal transducer according to one of the preceding claims, characterised in that the diameter of at least one of the openings (4.1 - 4.5) of the carrier layer (1) adjacent to the first active surface (10) on the first active surface (10) is a few µm up to a few mm, preferably some 10 - 100 µm.

25. Universal transducer according to one of the preceding claims, characterised in that the carrier has two cavities (4.2, 5.2, 6.2 and 4.4, 5.4, 6.4), a filling being disposed in each of the cavities, the filling of the one cavity being in contact with a first electrically conductive layer as reference electrode and the filling of the second cavity being in contact with second or third conductive layers, which are disposed on different carrier layers, as the operating electrode or counter electrode which are subject to a current, and the first,

second and third conductive layer forming a three electrode arrangement for amperometric measurements.

26. Universal transducer according to the preceding claim, characterised in that the carrier has a third cavity, in which a filling is disposed which is in contact with a further electrically conductive layer which forms a potentiometric electrode and is measurable against the reference electrode.

27. Use of universal transducers according to at least one of the preceding claims as reference electrode, as sensor element for potentiometric determination and/or as sensor element for amperometric determination of analyte concentrations or ion activities.

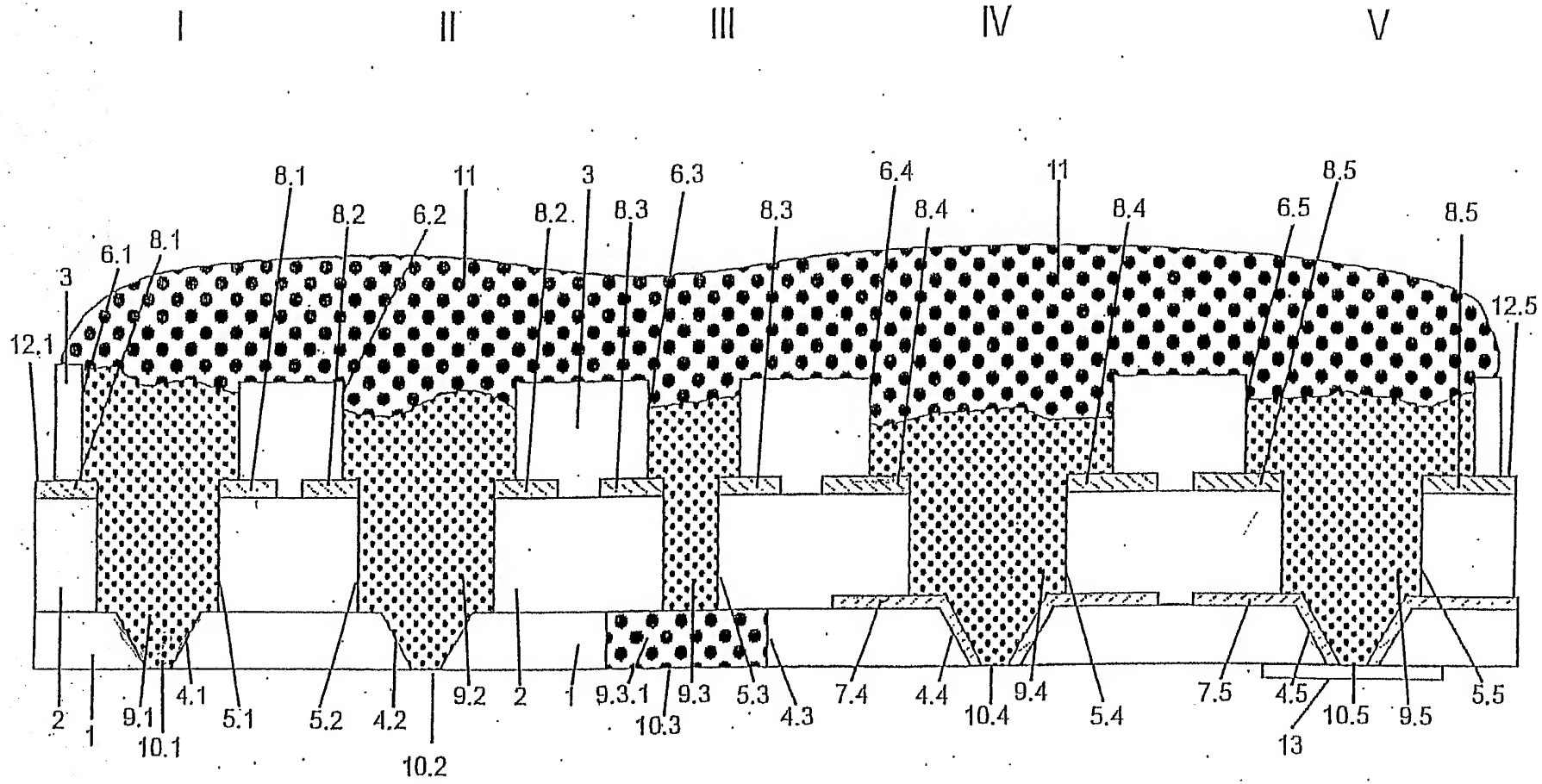
28. Use according to the preceding claim for determining the concentration of dissolved carbon dioxide, oxygen, glucose and/or other metabolites and/or urea or for determining the pH value or other parameters.

Abstract

The present application relates to a universal transducer and chemo- and biosensors based on miniaturised universal transducers of this type which are used for example in chemical analysis, medicinal diagnosis and the like for determining substance concentrations or ion activities in fluids.

The universal transducer according to the invention has a carrier which comprises at least two flat carrier layers (1, 2), each of the two carrier layers (1, 2) having at least one opening (4, 5). These openings (4, 5) form a continuous cavity which extends from a first active surface of the carrier over the first and the second carrier layer (1, 2). On the surfaces of at least one of the two carrier layers (1, 2), which surfaces are orientated away from the first active surface (10), there is disposed at least in part one electrically conductive layer which is in contact with a filling of the cavity.

(Figure 2c)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III
IV
V
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11
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8.3
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6.5
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6.1
8.1
3
12.1
12.5
2
1
9.1
10.1
4.1
5.1
5.2
4.2
10.2
9.2
2
1
9.3.1
10.3
9.3
5.3
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13
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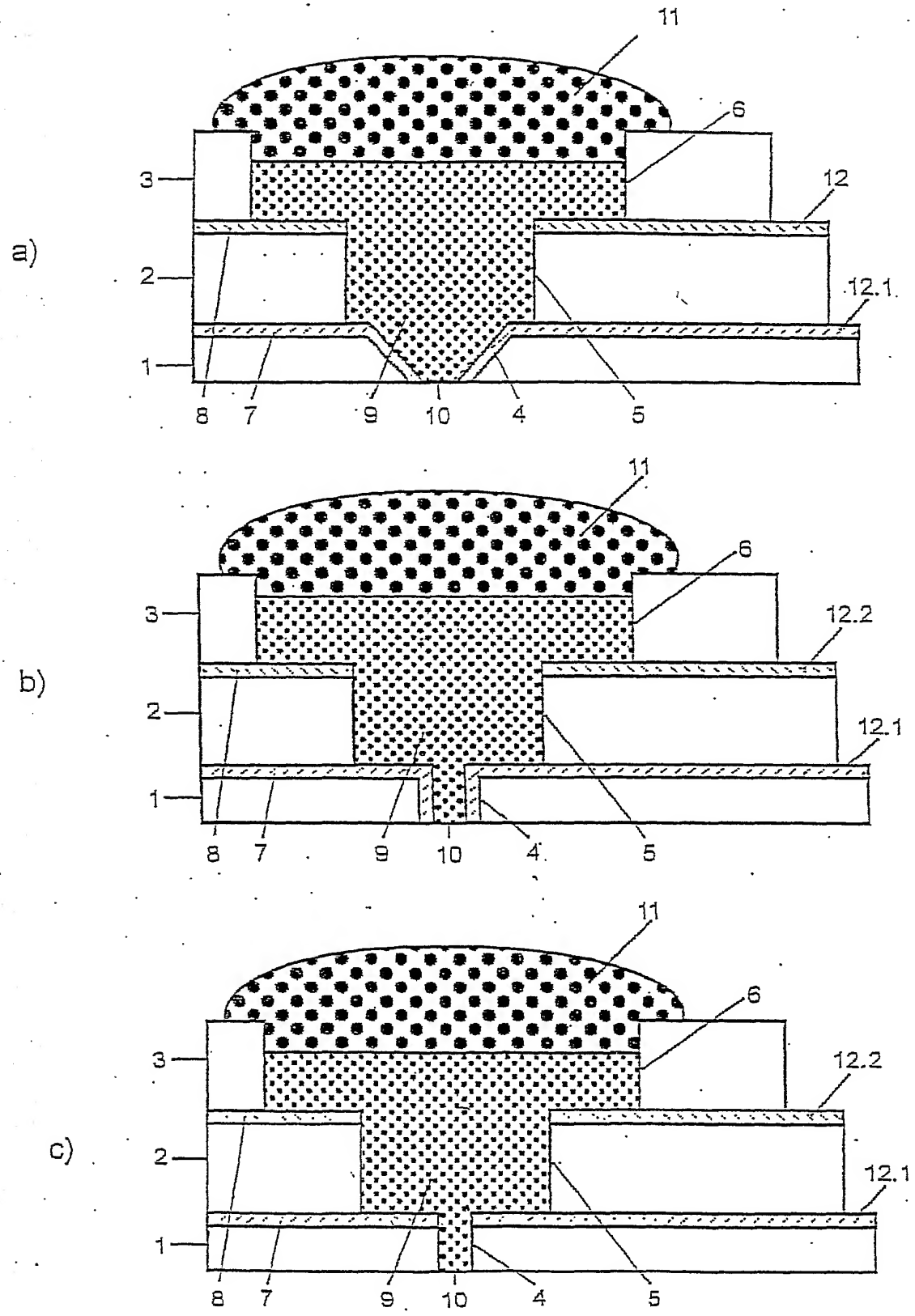
5.5

Fig. 1


a)
11
6
3
12
2
12.1
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8
7
9
10
4
5
b)
11
6
3
12.2
2
12.1
1
8
7
9
10
4
5
c)
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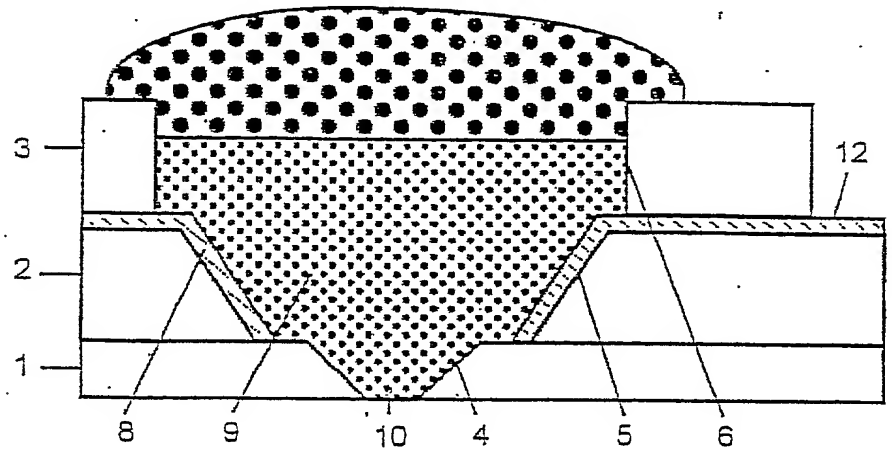
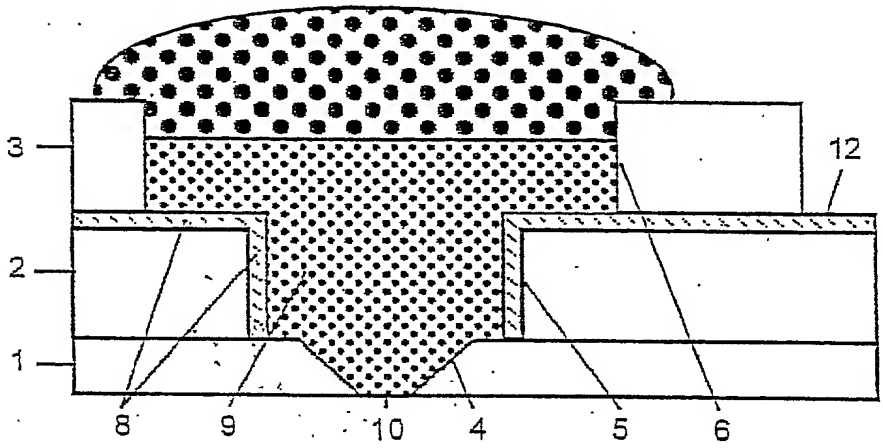
5

Fig. 2

a)



b)



c)

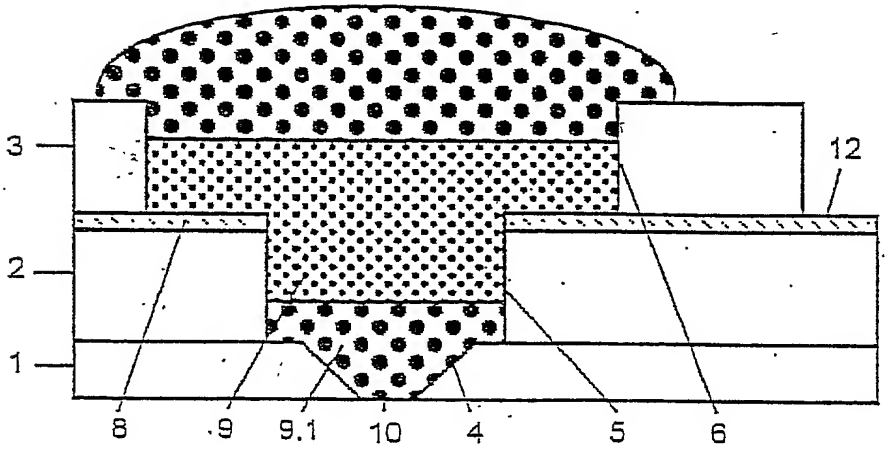


Fig. 3

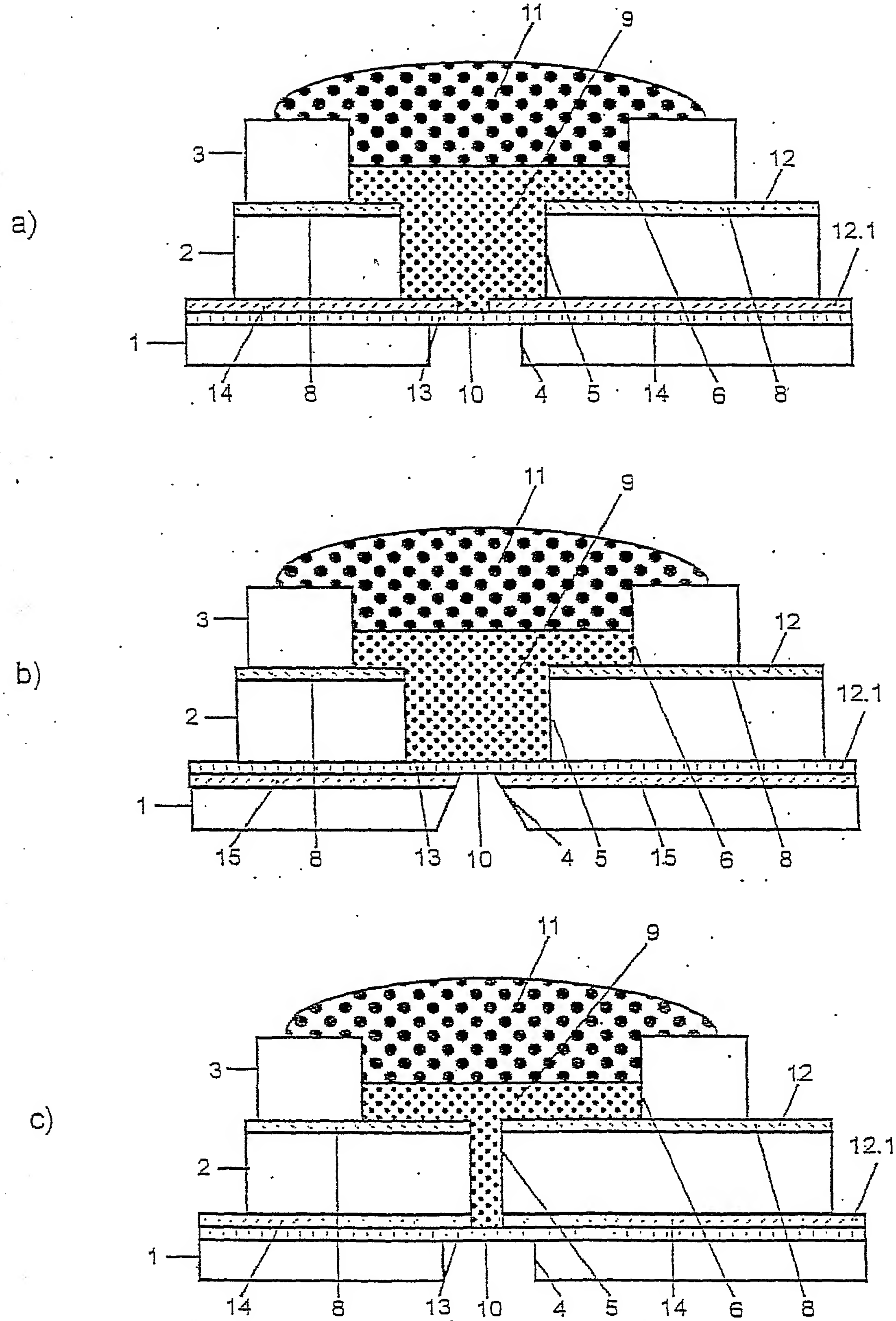


Fig. 4

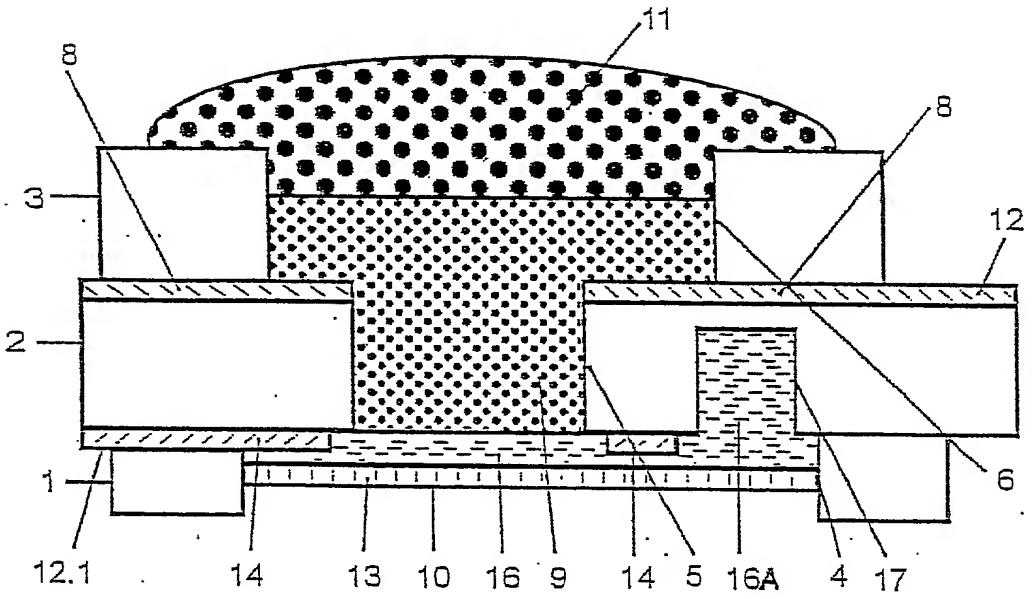


Fig. 5

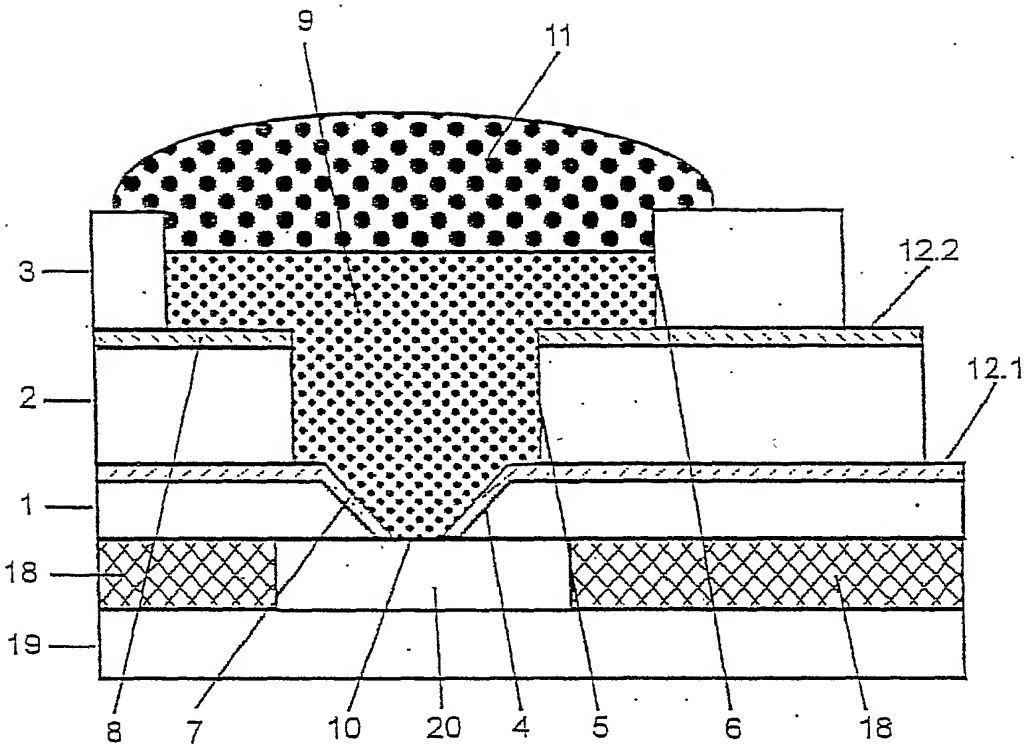


Fig. 6

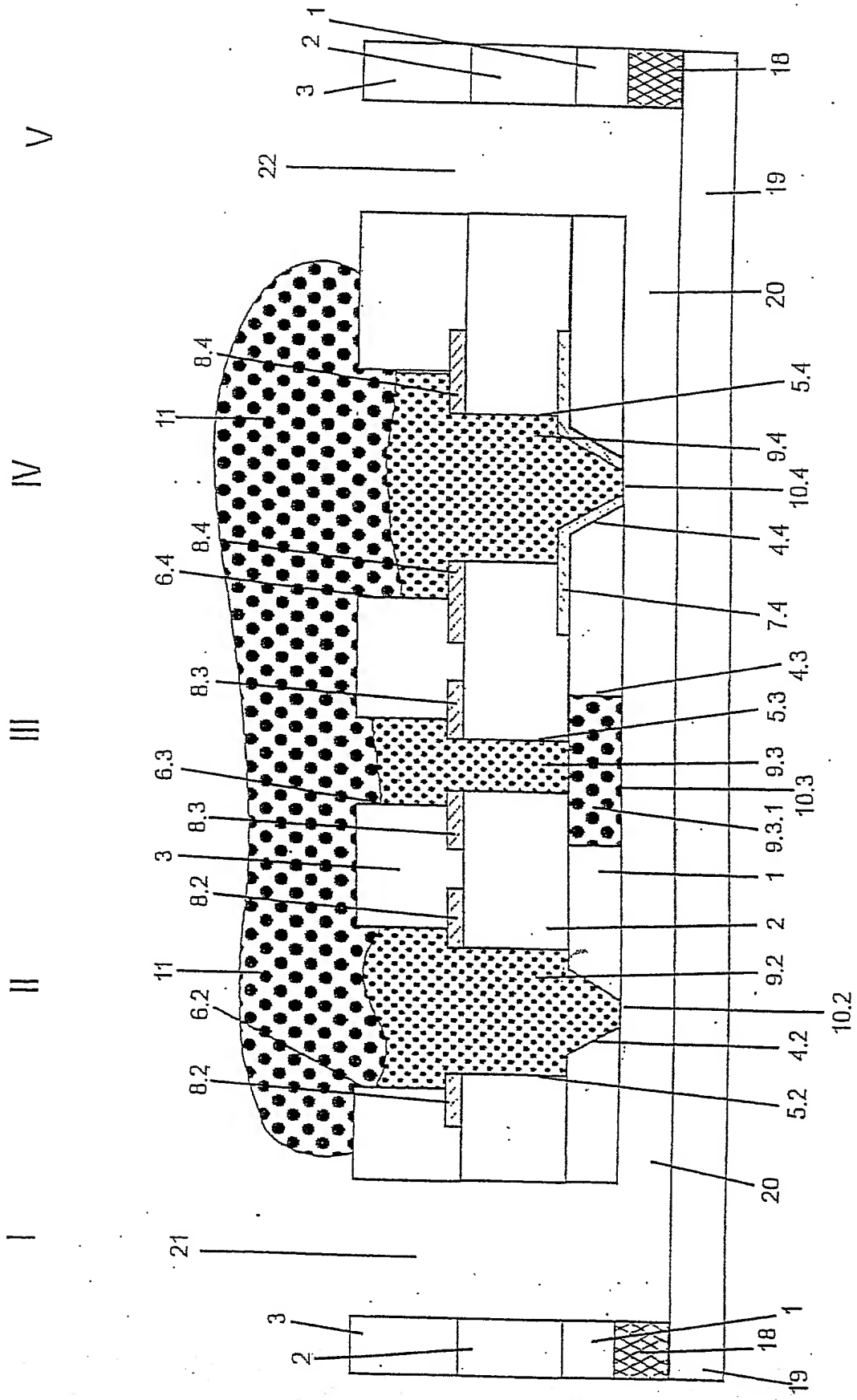


Fig. 7

#5

Our Reference: SPM-339-A

COMBINED DECLARATION AND POWER OF ATTORNEY

DECLARATION:

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

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the specification of which (check only one item below):

[ ] is attached hereto.

[ ] was filed as United States application Serial No. _____ on _____, and was amended on or through _____(if applicable).

[x] was filed as PCT international application Number **PCT/DE00/02003** on **June 15, 2000**, and was amended under PCT Article 19 on _____(if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate or §365(a) of any PCT international application(s) which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT international application(s) having a filing date before that of the application on which priority is claimed:

Prior Foreign/PCT Application(s) and any Priority Claims Under 35 U.S.C. §119:			Priority Claimed	
DE 199 29 264.7	**Germany**	**25/June/1999**	[X] Yes	[ ] No
(Number)	(Country)	(Day/Mo/Yr Filed)		
			[ ] Yes	[ ] No
(Number)	(Country)	(Day/Mo/Yr Filed)		

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

(Application Number)	(Filing Date)
(Application Number)	(Filing Date)

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or §365(c) of any PCT international application(s) designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

Prior U. S. Application(s) or PCT International Application(s) Designating the U.S. for Benefit Under 35 U.S.C. §120:

(Application Number)	(Filing Date)	(Status: patented, pending, abandoned)
(Application Number)	(Filing Date)	(Status: patented, pending, abandoned)

POWER OF ATTORNEY:

I hereby appoint the following attorney(s) and/or agent(s) Thomas N. Young, Patent Office Registration No. 20985, Andrew R. Basile, Patent Office Registration No. 24753, William M. Hanlon, Jr., Patent Office Registration No. 28422, Marshall G. MacFarlane, Patent Office Registration No. 30403, Donald L. Wood, Patent Office Registration No. 20014, Thomas D. Helmholdt, Patent Office Registration No. 33181, Todd L. Moore, Patent Office Registration No. 36874, Jason J. Young, Patent Office Registration No. 34048 and Darlene P. Condra, Patent Office Registration No. 37113 as my attorney(s) and/or agent(s), to prosecute this application and to transact all business in the United States Patent and Trademark Office connected therewith.

Send all correspondence to: **Andrew R. Basile**
Young & Basile, P.C.
3001 West Big Beaver Road, Suite 624
Troy, Michigan 48084
Phone: (248) 649-3333

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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